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Research Article

Insilico Studies of Chemical Constituents of Ocimum tenuiflorum for Anti-Diabetic Drug

D. P. Kawade*, N. B. Kureshi, S. M. Raut, M. R. Chaudhari, O. A. Lalzare, P. S. Mithe, N. T. Borkar

Priyadarshini J.L. College of Pharmacy, Electronic Zone, MIDC, Hingna Road, Nagpur, Maharashtra, India 440016

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ABSTRACT

In the present study, the anti-diabetic potential of Ocimum tenuiflorum was investigated using computational techniques for α-glucosidase, α-amylase, aldose reductase, and glycation at multiple stages. It aimed to elucidate the mechanism by which phytocompounds of O. tenuiflorum treat diabetes mellitus using concepts of druglikeness and pharmacokinetics, molecular docking simulations, molecular dynamics simulations, and binding free energy studies. Eugenol is a phenylpropene, propenyl-substituted guaiacol found in the essential oils of plants. During molecular docking modelling, isoeugenol was found to inhibit all the target enzymes, with a higher binding efficiency than standard drugs. Furthermore, molecular dynamic experiments revealed that isoeugenol was more stable in the binding pockets than the standard drugs used. Since our aim was to discover a single lead molecule with a higher binding efficiency and stability, isoeugenol was selected. In this context, our study stands in contrast to other computational studies that report on more than one compound, making it difficult to offer further analyses. To summarize, we recommend isoeugenol as a potential widely employed lead inhibitor of α-glucosidase, α-amylase, aldose reductase, and glycation based on the results of our in silico studies, therefore revealing a novel phytocompound for the effective treatment of hyperglycemia and diabetes mellitus.

INTRODUCTION

1.1. Drug Discovery and Development:

Discovery involves several processes like target identification and validation, hit identification, lead generation and optimization and finally the identification of a candidate for further development. Development, on the other hand, includes optimization of chemical synthesis and its formulation, toxicological studies in animals, clinical trials, and eventually regulatory approval.

***Corresponding Author:** D. P. Kawade
Address: *Priyadarshini J.L. College of Pharmacy, Electronic Zone, MIDC, Hingna Road, Nagpur, Maharashtra, India*
Email : d.kawade@pjlcp.edu.in

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Both processes are time-consuming and expensive and currently the industry is under pressure owing to the extremely stringent regulatory requirements, environmental concerns, and reduced incomes due to patent expirations. These issues have had an adverse bearing on the R&D productivity in recent years; hence there is a need for innovative approaches as well as increased collaboration between industry, academia, and governmental research institutions, with a common objective of constantly delivering quality medicines. This chapter will look at the preclinical discovery stage in detail along with highlighting the development processes. Additionally, it will also touch upon the issues faced by the pharmaceutical industry and the newer approaches which have the potential to ensure the future sustainability of the pharmaceutical industry.[1]

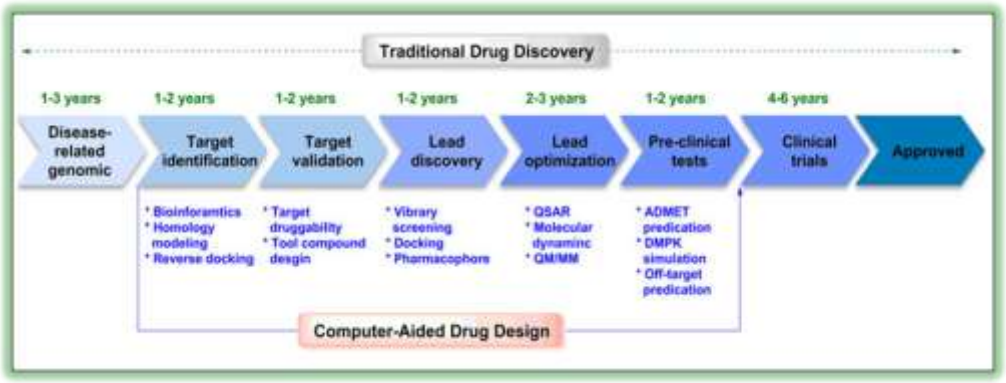


Fig.no. 1: Drug Discovery and Development

Today's fast moving pharmaceutical market requires more efficient drug development and production. Pharmaceutical development is intended to design a quality product and a manufacturing process that can consistently deliver the product with its intended performance. A pharmaceutical product should be designed to meet patients' needs. The knowledge and information acquired from pharmaceutical development studies and manufacturing experience offer scientific understanding to support the establishment of the design space, specifications, and manufacturing controls. A more systematic approach to development (also defined as quality by design) can include, for example, incorporation of prior knowledge, results of studies using design of experiments, use of quality risk management, and use of knowledge management throughout the lifecycle of the product. The present chapter focuses on the key areas of pharmaceutical development currently followed in the pharmaceutical industry.[2]

1.2. Stages of Drug Discovery and Development include

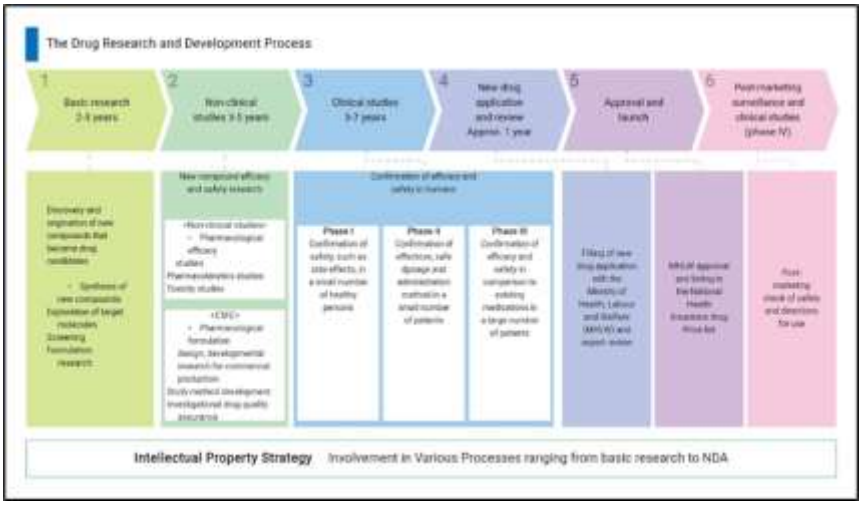


Fig.2: Drug Discovery Process

Stages of Drug Discovery and Development include

- Target identification
- Target validation
- Lead identification
- Lead optimization
- Formulation and development
- Preclinical research
- Investigational new Drug
- Clinical Trial
- New drug Application
- Approval

Target Identification:

Target identification is the initial phase of drug discovery. A biological target is an element or technique that has an effect in a certain illness.

Any biological mechanism essential to the development of the disease, whether it be a protein, enzyme, gene, or any other, might be the cause of the disease (3)

Potential targets are discovered by scientists using a variety of methods, including genetic and biochemical methodologies, epidemiological research, and clinical observations.

Target Validation:

New target validation is the basis of completely new drug exploration and the initial step of drug discovery. New drug target validation might be of great help not only to new drug research and development but also provide more insights into pathogenesis of target related disease. Target validation is the process of demonstration the function role of the identified target in the disease phenotype.

Lead Discovery:

The subsequent stage in drug development is lead discovery, which comes after a potential target has been located. A chemical that interacts with the target and has positive pharmacological action is called a lead compound. Lead discovery can be accomplished using a variety of methods, including as high-throughput screening, virtual screening, and natural product screening.

High-throughput screening includes searching through huge chemical libraries for molecules that interact with the target. Robotic systems that can test tens of thousands of chemicals each day are used for this (4)

Virtual screening is the process of determining which chemicals are most likely to interact with the target based on its structure and attributes using computer simulations.

Natural product screening includes looking for molecules that interact with the target in natural goods, such as plant extracts or microbial cultures

Lead Optimization:

Lead optimization is the subsequent phase of drug development after the identification of a lead molecule. To increase the lead compound's pharmacological activity, selectivity, and safety, the structure must be modified. Lead optimization can be done using a variety of methods, including as medicinal chemistry, structural biology, and pharmacology.

In medicinal lead compound's chemical structure may need to be slightly altered in order to increase potency and chemistry, novel molecules that have a structural similarity to the lead chemical are synthesized and tested.

In structural biology, the three-dimensional structure of the target and how it interacts with the lead molecule are ascertained using X-ray crystallography and other methods. Designing novel substances that modulate the target more successfully can be done using this knowledge. Pharmacology involves investigating the lead compounds pharmacokinetic, Pharmacodynamic and safety characteristics in preclinical models.

Formulation and development

Pharmaceutical formulation is a stage of drug development during which the physiochemical properties of active pharmaceutical ingredients (APIs) are characterized to produce a bioavailable stable and optimal dosage form for specification administration route [5]

Preclinical Research

Preclinical testing is necessary before a lead chemical can be evaluated on humans. Preclinical Testing entails examining the drug's pharmacokinetics, effectiveness, and safety in animal models. Preclinical testing aims to spot any possible safety issues and establish the best dose and dosing schedule for the compound in question.

Investigational new drug Application (INDA)

INDA is applied after the preclinical studies show success and if the INDA submission is accepted the product further forwarded to the clinical research studies (phase 1-4)

Clinical Research

Clinical trials are a crucial part of the process of developing novel drugs. They are made to examine a prospective new medication's pharmacokinetics, effectiveness, and safety in human test participants.

Phases of clinical trials are carried out, with each phase intended to address particular questions regarding the safety and effectiveness of the medicine.

Phase I Clinical Trials - Healthy Volunteer Study

- Phase I clinical trials are the initial step of a possible new drug's clinical testing.
- These tests are often carried out on healthy volunteers to assess the drug's pharmacokinetics, safety, and tolerability [6]
- Phase I clinical trials' main goals are to ascertain the drug's maximum tolerable dose and to pinpoint any negative effects or side effects.

- Small volunteer groups, usually between 20 and 80 people, are used for phase I clinical studies.
- Depending on the pharmacokinetics of the medicine and the number of doses being evaluated, these studies may continue for a number of weeks or months.
- Participants in phase I clinical trials are constantly watched for side effects and regularly tested for blood and urine to assess the pharmacokinetics of the medicine.

Phase II Clinical Trials- Studies In Patient Population

- Phase II clinical trials are the second stage of a possible new drug's clinical testing.
- Usually, just a few people with the target disease or condition are used in these trials.
- Phase II clinical trials' main goal is to assess the drug's effectiveness and safety in human subjects.
- Phase II clinical studies might involve several hundred individuals and are often larger than phase I trials [171]
- Depending on the effectiveness of the treatment and the number of dosages being evaluated, these studies may run several months to a few years.
- Phase II clinical trial participants are constantly watched for side effects and regularly subjected to imaging and blood testing to gauge the drug's effectiveness.

Phase III Clinical Trials

- Phase III clinical trials are the last step of a possible new drug's clinical testing.
- The target ailment or condition is often tested in these studies on a sizable number of people.
- Phase III clinical trials' main goals are to determine any unusual or long-term side effects and to establish the medication's effectiveness and safety in a broader patient group.
- Phase III clinical studies can involve thousands of people and are often substantially bigger than phase II trials.
- To guarantee a broad patient group, these studies frequently extend many years and take place at numerous different locations.
- Participants in phase III clinical trials are rigorously watched for side effects and regularly subjected to imaging exams, blood tests, and other evaluations to determine the effectiveness and safety of the medication.

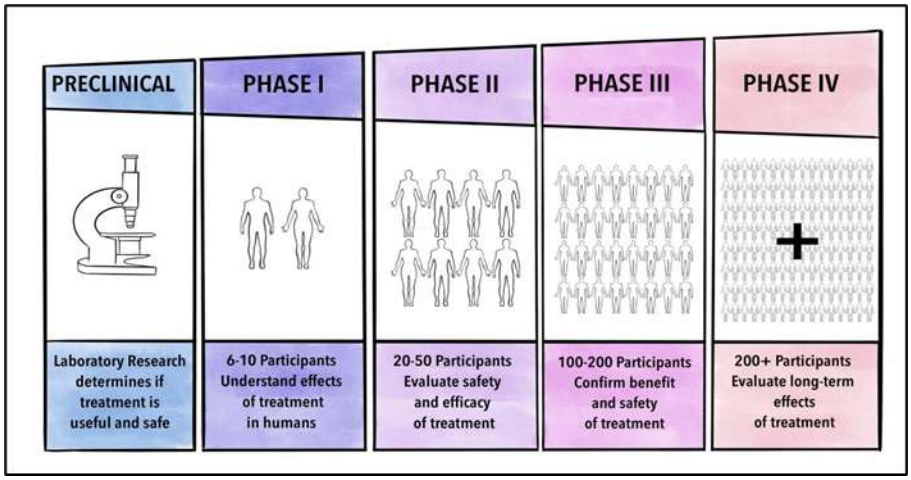


Fig.no. 3. Phases of clinical trial

New Drug Application (NDA)

A New Drug Application expresses the full story of a drug molecule. Its purpose is to verify that a drug is safe and effective for its purpose use in the people studied. A drug developer must include all about a drug starting from preclinical data to phase 3 trials to NDA. Developer must include all the study, data, and analysis.

Approval

In cases where FDA determines that a drug has been shown to be safe and effective for its intended use, it is necessary to work with the applicant to develop and refine prescribing information. This is referred as labeling. Labeling accurately and objectively describes the basic for approval and how approval and how best to use of drug Often, through, remaining issues need to be resolve before the drug can be approved for marketing sometime FDA require the developer to address questions based on existing data.

1.3 . Computer aided drug design:

CADD (computer aided drug design) is a technique which uses software for predicting the structure value of properties of known, unknown, stable and unstable molecular species using mathematical equations. Computers are essential tool in modern chemistry and are important in both drug discovery and development. Computers are essential tool in modern chemistry and are important in both drug discovery and development. Structure-based drug design (SBDD) and ligand-based drug design (LBDD) are the two general types of computer-aided drug design (CADD) approaches in existence. [8,9]

Computational tools have become increasingly important in drug discovery and design processes. Methods from computational chemistry are used routinely to study drug-receptor complexes in atomic detail and to calculate properties of small-molecule drug candidates. Tools from information sciences and statistics are increasingly essential to organize and manage the huge chemical and biological activity databases that all pharmaceutical companies now possess, and to make optimal use of these databases. In addition, the act of generating chemical derivatives is highly amenable to computerized automation A computer can rapidly generate and predict the binding of all potential derivatives, creating a list of best potential candidates. In essence, the computer filters all weak binding compounds, allowing the chemist to focus, synthesize, and test only the most promising ligands. Thus, using the CADD software to aid in the refinement of lead molecules

is the most effective manner in which these tools can be employed.

Applications have been shown to be effective tools, and notable successes have been achieved Computers have found their way in every field of science and technology today. Drug designing has received a many folds face-lift by the virtue of computer software dedicated to the designing of ligands and identifying the biological targets. Computer generated structures serve to be good predictive models for the evaluation of biological activity. A drug exhibits its action when it binds to its biological target, usually receptors. Receptors are nothing but proteins with active sites for the binding of ligands. Hence, in order to design a good ligand, it becomes necessary to know the structure of such receptors and to identify their active sites accurately.

The two important aspects involved in predicting molecular-interactions in computer-aided drug design (CADD) are development of pharmacophore-based and molecular docking and scoring techniques. Computerized structure of the known proteins is based on the experimental data present in various literatures and protein data banks. With this, it is possible to deduce the 3D structure of all the known proteins with the help of sequence homology approach. Hence, these hypothetical proteins behave more or less like the real proteins in their native biological environment.

A combination of advanced computational techniques, biological science, and chemical synthesis was introduced to facilitate the discovery process, and this combinational approach enhanced the scale of discovery. whereby different computational methods are used to simulate interactions between receptors and drugs in order to determine binding affinities. An overview of CADD is provided in. CADD may be broadly categorized embracing both structure- and ligand-based drug designs. Illustrates various approaches applied in CADD. [10]

Various approaches applied in CADD.

- Molecular Dynamics
- Virtual Screening
- Molecular Docking
- Molecular Modelling
- QSAR
- SAR
- Pharmacophore modling

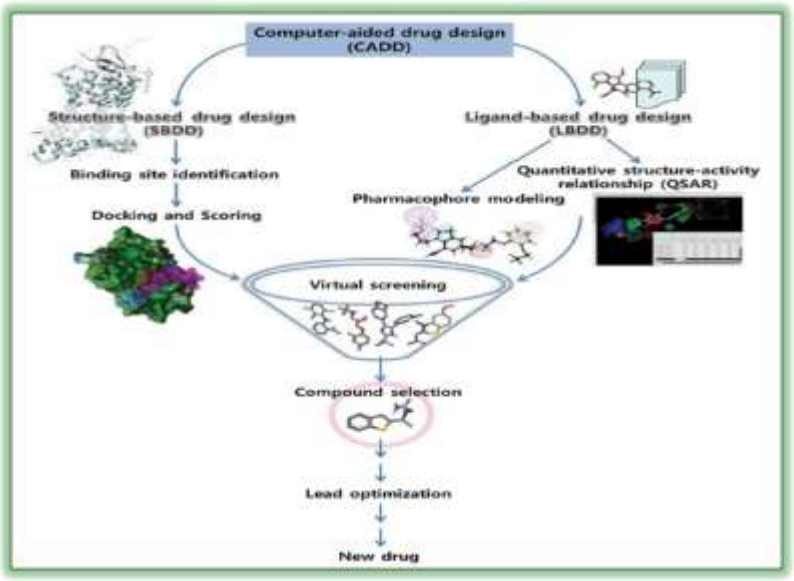


Fig no.4 Computer aided drug design

1.4. Molecular Docking

Molecular docking is a key tool in structural molecular biology and computer-assisted drug design. The goal of ligand-protein docking is to predict the predominant binding mode of a ligand with a protein of known three-dimensional structure. Successful docking methods search high-dimensional spaces effectively and use a scoring function that correctly ranks candidate dockings. The main objective of molecular docking is to attain ligand-receptor complex with optimized conformation and with the intention of possessing less binding free energy.

Docking can be used to perform virtual screening on large libraries of compounds, rank the results, and propose structural hypotheses of how the ligands inhibit the target, which is invaluable in lead optimization. The setting up of the input structures for the docking is just as important as the docking itself and analysing the results of stochastic search methods can sometimes be unclear. This chapter discusses the background and theory of molecular docking software and covers the usage of some of the most-cited docking software. Practical application of molecular docking requires data bank for the search of target with proper PDB format and a methodology to prepare ligand as a PDB file. To do this, there are various software's Discovery studio, etc., available from where the ligand can be made in PDB format. The molecular docking approach can be used to model the interaction between a small molecule and a protein at the atomic level, which allow us to characterize the behavior of small molecules in the binding site of target proteins as well as to elucidate fundamental biochemical process [11,12]

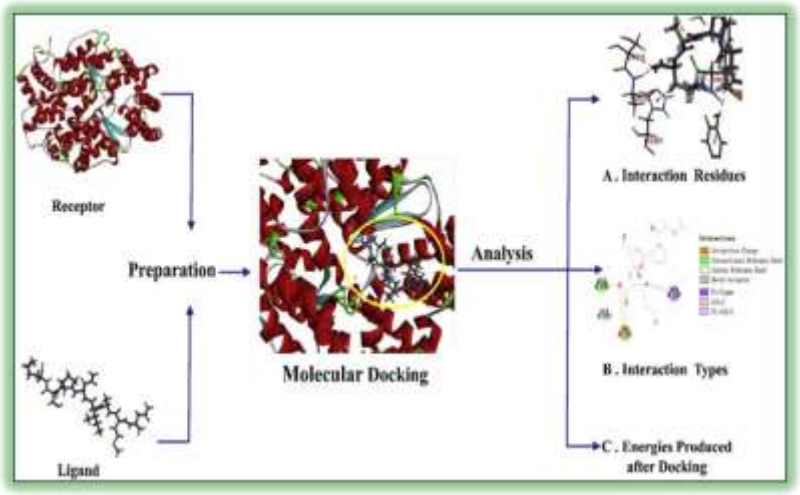


Fig.no.6: Molecular Docking

Types of Molecular docking

1. Rigid Docking

2. Flexible Docking

Rigid Docking

Assuming the compounds are inflexible, we are seeking a rearrangement of one of the compounds in three-dimensional space that results in the best match to the other compounds in parameters of a scoring system. Assuming the compounds are inflexible, we are seeking a rearrangement of one of the compounds in three-dimensional space that results in the best match to the other compounds in parameters of a scoring system.

Flexible Docking

In conjunction with transformation, we evaluate molecular flexibility to identify confirmations for the receptor and ligand molecules as they exist in the complex.[13]

1.5. Diabetic mellitus:

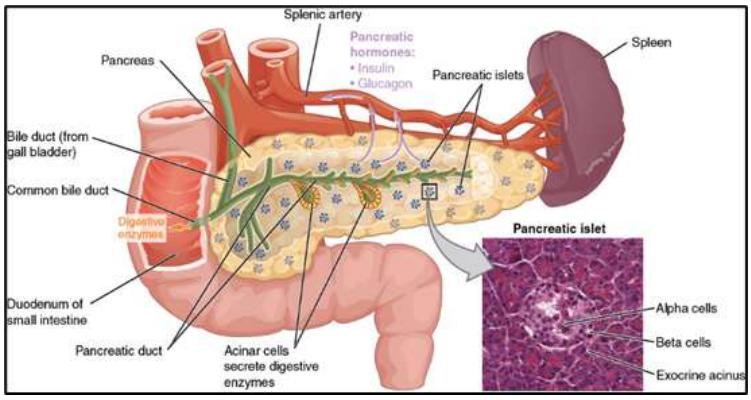


Fig.no. 7 Diabetic mellitus

Diabetes Mellitus is a chronic metabolic disorder in which the level of glucose (sugar) in the blood becomes higher than normal. This happens when the body either does not produce enough insulin or cannot use insulin properly.

Insulin is a hormone produced by the pancreas that helps glucose enter the cells to be used for energy.

Types of Diabetes

1. Type 1 Diabetes

The body does not produce insulin

Usually occurs in children or young adults

Requires insulin therapy

2. Type 2 Diabetes

The body cannot use insulin effectively (insulin resistance)

Most common type

Linked with lifestyle and obesity

3. Gestational Diabetes

Occurs during pregnancy

Usually disappears after delivery

Symptoms

- Some people may not show symptoms early, but common symptoms include:
- Frequent urination
- Increased thirst
- Increased hunger
- Fatigue
- Blurred vision
- Slow healing of wounds
- Unexplained weight loss

Causes

Diabetes occurs when:

- The pancreas does not produce insulin
- Or the body cannot use insulin properly

Common causes include:

- Genetic factors (family history)
- Obesity
- Lack of physical activity
- Unhealthy diet

Risk Factors

- Overweight or obesity
- Age above 40 years
- Family history of diabetes
- Sedentary lifestyle
- High blood pressure
- Poor eating habits

Complications

- If not controlled, diabetes can lead to:
- Heart disease
- Kidney damage
- Nerve damage
- Eye problems (retinopathy)

Prevention and Treatment

- Lifestyle Management

- Balanced diet (low sugar, high fiber)
- Regular physical activity
- Maintaining healthy body weight

Medicinal Treatment (Anti-diabetic Drugs)

1. Oral Drugs

- Metformin (first-line treatment)

- Sulfonylureas (increase insulin secretion)

2. Insulin Therapy

- Required in Type 1 diabetes

- Used in advanced Type 2 diabetes

3. Other Medications

- DPP-4 inhibitors

- GLP-1 receptor agonists

1.6. Ocimum tenuiflorum (Tulsi):



Fig.no. 8. Ocimum

Kingdom: Plantae

Family: Lamiaceae

Genus: Ocimum

Species: O. tenuiflorum

Order: Lamiales

Since ancient times, medicinal plants have been widely used in traditional systems of medicine for the treatment of various diseases. In recent years, herbal medicine has gained importance as an alternative or complementary therapy due to its lower cost, better safety profile, and minimal side effects compared to synthetic drugs.

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to insulin deficiency or resistance. Long-term uncontrolled diabetes leads to serious complications such as neuropathy, nephropathy, and cardiovascular diseases. Therefore, there is a growing interest in identifying plant-based compounds with anti-diabetic potential.

Ocimum tenuiflorum (Tulsi) is a well-known medicinal plant rich in bioactive phytoconstituents such as eugenol, ursolic acid, rosmarinic acid, and flavonoids, which have shown promising anti-diabetic activity. [13,14,15]

Phytoconstituents (Active Compounds)

Tulsi contains many bioactive compounds responsible for anti-diabetic activity:

Eugenol

Ursolic acid

Rosmarinic acid

Flavonoids

Tannins

Saponins

These compounds help reduce blood sugar and improve insulin function.

Mechanism of Anti-Diabetic Action

Tulsi works through multiple mechanisms:

1. Insulin Secretion Enhancement

Stimulates pancreatic β-cells

Increases insulin production

2. Reduction of Blood Glucose

Decreases fasting blood sugar

Improves glucose tolerance

3. Antioxidant Activity

Reduces oxidative stress (important in diabetes complications)

4. Inhibition of Carbohydrate Metabolism Enzymes

Inhibits enzymes like α-amylase and α-glucosidase

Slows down glucose absorption

5. Improves Lipid Profile

Reduces cholesterol and triglycerides

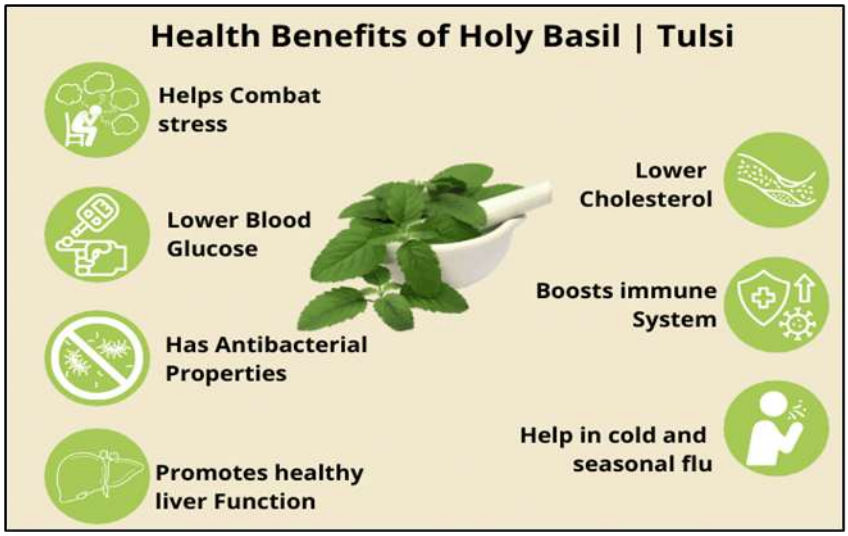


Fig. no. 9 Benefits of Ocimum tenuiflorum

2. AIM AND OBJECTIVE

AIM:

For the treatment of Diabetes Mellitus, various drugs are used but they may cause side effects. The aim of this study is to identify a lead molecule from the phytoconstituents of Ocimum tenuiflorum as an anti-diabetic agent with minimum side effects.

OBJECTIVE:

The objective of this project is to perform in silico studies of phytoconstituents of Ocimum tenuiflorum as anti-diabetic agents by molecular docking with target proteins such as DPP-4, α-glucosidase, and PPAR-γ for the treatment of Diabetes Mellitus.

3. EXPERIMENTAL WORK

3.1 DOWNLODING SOFTWARE PROGRAME:

CHEMSKETCH: ChemSketch is a molecular modeling program used to create and modify images of chemical structures. Also, there is software that allows molecules and molecular models displayed in two and three dimensions, to understand the structure of chemical bonds and the nature of the functional groups. Use to draw the structure of drug molecule to fine out the IUPAC name of the unknown compound, to find out structure of drug name from its IUPAC NAME & SMILE of unknown drug.

AVAGADRO Software is a molecule editor and visualize designed for cross platform use computational chemistry, molecular modeling, etch and also used to convert a mol. file, pdb format.

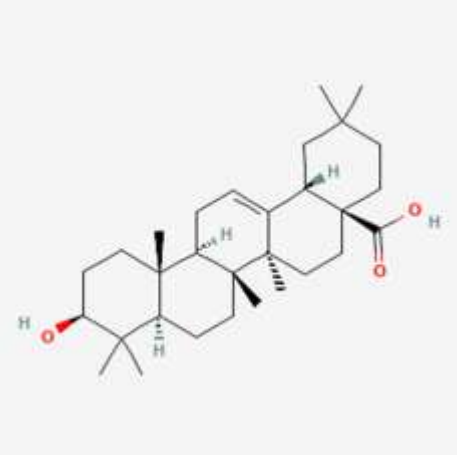
PYRX software is virtual screening software for computational drug discovery that can be used to screen libraries of compounds against potential drug targets. Discovery studio was use molecular inaction and visualization.

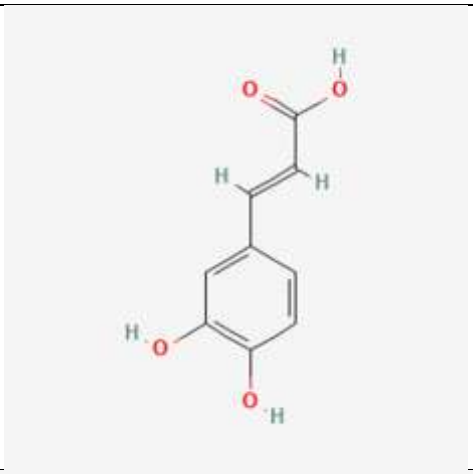
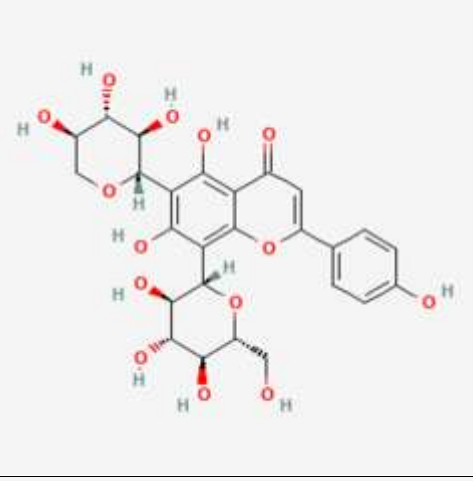
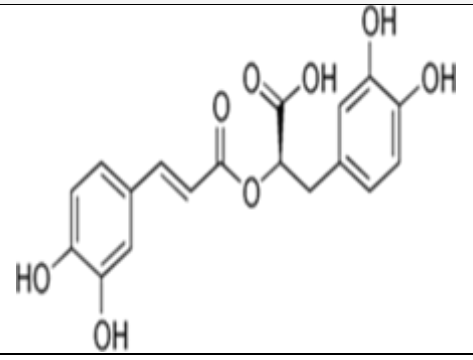
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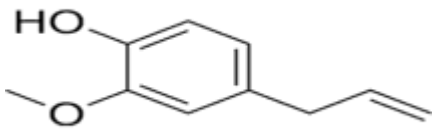
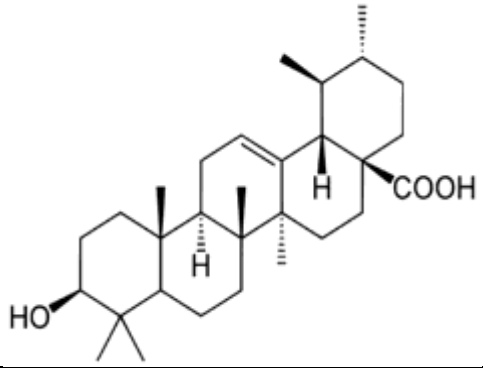
3.2 PREPARATION OF LIGAND

In this study, Curcuma longa, commonly known as Turmeric, was chosen for its Anti-ulcer Properties. Various phytochemical present in turmeric contributes to its therapeutic effects. To understand further select phytoconstituents using ChemSketch software and then the structure was cleaned and then structure was saved in the working folder as mol file. This mol file was then accessed in Avogadro Software tool in which that the mol file is convert to. Pdb format and then the structure was optimized by using the optimization tool and then saved the optimized structure in the working directory as.pdb file.

Table No.1. Phytoconstituent of Ocimum Tenuiflorum

Sr. No	Ligands	IUPAC Name	2D Structure
1	OLEANOLIC ACID	(4aS,6aR,6aS,6bR,8aR,10S,12aR,14bS)-10-hydroxy-2,2,6a,6b,9,9,12a-heptamethyl-1,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydropicene-4a-carboxylic acid	

2	Caffeic Acid	(E)-3-(3,4-dihydroxyphenyl)prop-2-enoic acid	
3	Vicenin	5,7-dihydroxy-2-(4-hydroxyphenyl)-8-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]-6-[(2S,3R,4S,5R)-3,4,5-trihydroxyoxan-2-yl]chromen-4-one	
4	Voglibose	(1S,2S,3R,4S,5S)-5-(1,3-dihydroxypropan-2-ylamino)-1-(hydroxymethyl)cyclohexane-1,2,3,4-tetrol	
5	Rosmarinic acid	(2R)-3-(3,4-dihydroxyphenyl)-2-[(E)-3-(3,4-dihydroxyphenyl) prop-2-enoyl]ox propanoic acid	

6	Eugenol	2-methoxy-4-prop-2-enylphenol	
7	Urosolic acid	S,2R,4aS,6aR,6aS,6bR,8aR,10S,12aR,14bS)-10-hydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydro-1H-picene-4a-carboxylic acid	

3.3 Preparation of Receptor

Histamine causes inflammation and hemorrhage, hastening the appearance of ulcer and produces more serious H2 receptor antagonisis effectively block H2 recepíoı oı paticial cells. Leading to the inhibition of gastric acid production They also mitigate acid stimulation triggered by acetylcholine, gastric and food, among other factors. Consequently, H2 blockers were chosen as the subject of drug studies, with the H2 receptor serving as the primary target for intervention. The 3D structure of the receptor having ID-7ul3 was obtained from the RCSB PDB database in PDB format. Subsequently, the downloaded structure underwent preparation for docking in Discovery Studio. This involved removing ligands, cofactor, heteroatom's, ion, etc. from the receptor structure. Optimization and energy minimization procedure were then conducted to enhance the stability and accuracy of the receptor structure, which was ultimately downloaded in PDB format for further analysis and study for further docking process. [16][17]

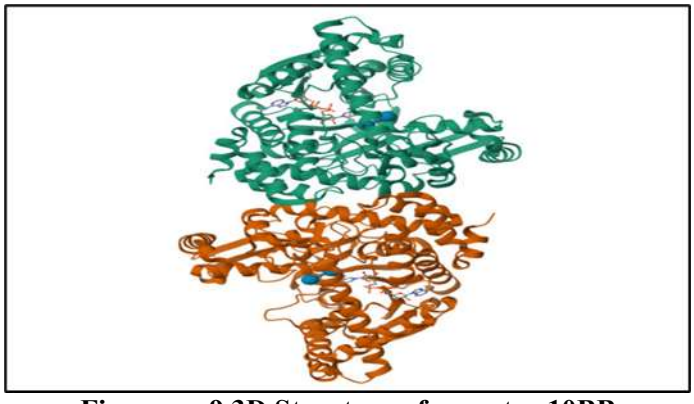


Figure no.9 3D Structure of receptor 10BB

3.4 Physicochemical Properties

Lipinski rule was used to assess the physiochemical properties of all the selected

ligands and to predict their drug like properties, and the Swiss ADME as used to compute the SMILE structure of each compound.

3.5 ADME Studies

ADME (Absorption, Distribution, Metabolism and Excretion) studies are indeed crucial in drug development to assess how a drug behaves within the body. Swiss ADME software was used to determine these properties of each ligand.

3.6 Druglikeness

To be effective as a drug, a potent molecule must reach its target in the body in sufficient concentration, and stay there in a bioactive form long enough for the expected biologic events to occur. Drug development involves assessment of absorption, distribution, metabolism and excretion (ADME) increasingly earlier in the discovery process, at a stage when considered compounds are numerous but access to the physical samples is limited. In that context, computer models constitute valid alternatives to experiments. Here, we present the new SwissADME web tool that gives free access to a pool of fast yet robust predictive models for physicochemical properties, pharmacokinetics, drug-likeness and medicinal chemistry friendliness, among which in-house proficient methods such as the BOILED-Egg, ¡LOGP and Bioavailability Radar. Easy efficient input and interpretation are ensured thanks to a user-friendly interface through the login-free website http://www.swissadme.ch.

3.7 Toxicity Study

Protox 3.0 is a powerful tool in the realm of computation toxicology, offering predictive insights into the potential toxicity of various chemical compounds, particularly ligands. It analyses the structural properties of provided ligands to

forecast their toxicity profiles. Thus, it was used to determine the toxicity profile of ligands. [18]

3.8 Molecuiar Docking

Molecular docking using PyRx is a powerful computational technique employed to predict the binding interaction between a set of ligand and a target receptor molecule.

In Silico Studies of Phytoconstituents of Curcuma longa as II, Receptor locker for Treatment of Peptic Ulcer is integral to drug discovery and design, as it aids in identifying potential lead compound with high binding affinity and favorable interaction patterns.

To perform molecular docking using PyRx:

1. Improve structure into PyRx: The receptor structure (usually in PDB format) and the ligand structure (in formats such as PDB, MOL2 or SDF) were imported in PyRx.

2. Defining the Binding site: The binding site or active site within the receptor was specified were the ligands are expected to interact by defining the grid box. This helps in focusing the docking calculation on the relevant region of receptor.

3. Setting Docking Parameters: Configure the docking poses to generate. This parameter influences the accuracy and efficiency of the docking calculations.

4. Performing Molecular Docking: The docking process was initiated. The software systematically explores the conformational space of each ligand and predicts its binding poses within the defined binding site of receptor.

5. Analyzing Docking Results: After Docking is complete, PyRx provides a list of docking poses for each ligand, along with their corresponding binding energies. The docked complexes with visualized to analyze the interaction between the ligand and the receptor, such as hydrogen interaction, and electrostatic interactions.

6. Lead Compound Selection: The docking results are evaluated to identify lead compound that exhibit the most favourable binding affinity and interaction patterns. This lead compound can be prioritized validation and optimization.

7. By utilizing PyRx for molecular docking, researcher can efficiently screen large libraries of ligands and gain valuable insights into their binding interaction with target receptor. This computation approach accelerates the drug discovery process by narrowing down the pool of potential lead compound and guiding subsequent experimental efforts.

4. RESULTS AND DISCUSSION

1. Physicochemical properties

The physicochemical properties of the compounds were studied to predict the pharmacokinetics of the drugs, using Lipinski's rule. Lipinski's rules describe orally active drug compounds as having a molecular weight (MW) of < 500 Da, an octanol-water partition coefficient (Log P) of 5, a polar surface area (PSA) of < 150 A, number of hydrogen bond donors (HBDs)< 5 number of hydrogen bond acceptors (HBAs)< 10 , and number of rotatable bonds (RBs) < 10 The Lipinski values for each of the selected compounds are listed in

Table No.2. Physicochemical Properties of Ligands

Sr. No	Ligands	No. of rotatable bonds	No. of H-bond accept	No. of H-bond donors	Molar refractivity	Molecular Weight (g/mol)	TPSA
1	Rosmarinic acid	7	8	5	91.40	360.31	144.52
2	Ursolic acid	1	3	2	136.91	456.50	57.53
3	Eugenol	3	2	1	49.06	164.20	29.46
4	Caffeic acid	2	4	3	47.60	180.16	77.76
5	Oleanolic acid	1	3	2	136.91	456.70	57.53
6	Vicenin	4	14	10	133.26	564.49	250.97
7	Voglibose	5	8	8	59.04	267.28	153.64

2. ADME Properties

Table No.3. Pharmacokinetics Properties of Ligands

Sr. No	Ligands	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2D6 inhibitor	Log Kp (cm/s)
1	Rosmarinic acid	LOW	NO	NO	NO	NO	-6.82
2	Ursolic acid	LOW	NO	NO	NO	NO	-3.87
3	Eugenol	HIGH	YES	NO	YES	NO	-5.69
4	Caffeic acid	HIGH	NO	NO	NO	NO	-6.58
5	Oleanolic acid	LOW	NO	NO	NO	NO	-3.77
6	Vicenin	LOW	NO	YES	NO	NO	-11.30
7	Voglibose	LOW	NO	YES	NO	NO	-10.83

3. Druglikeness

Table No.4. Drug likeness Properties of Ligands

Sr. No	Ligands	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability score
1	Rosmarinic acid	YES	YES	NO	NO	YES	0.56
2	Ursolic acid	YES	NO	YES	NO	NO	0.85
3	Eugenol	YES	YES	YES	YES	NO	0.55
4	Caffeic acid	YES	YES	YES	YES	NO	0.56
5	Oleanolic acid	YES	NO	YES	NO	NO	0.85
6	Vicenin	NO	NO	NO	NO	NO	0.17
7	Voglibose	YES	NO	NO	NO	NO	0.55

4. Toxicity Studies

Table No.5. Toxicity Study of Ligand

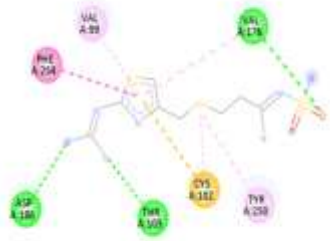
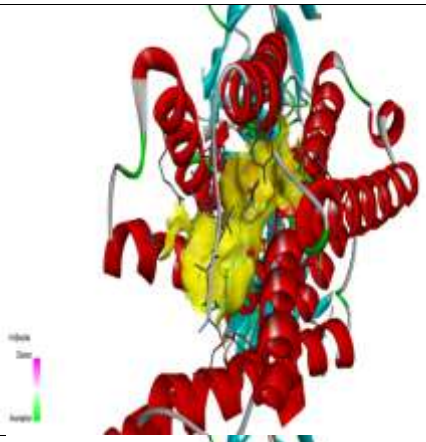
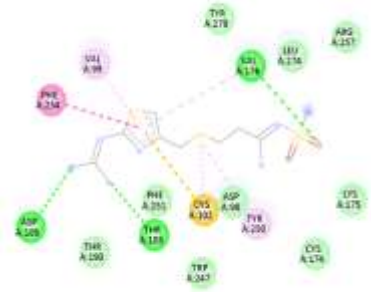
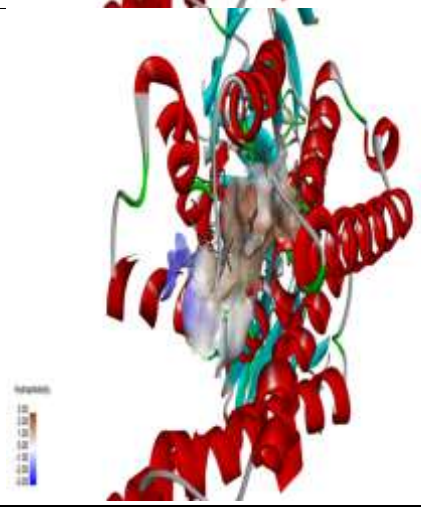
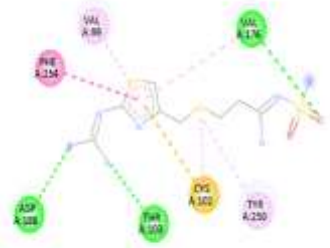
Sr. No	Ligands	Predicted Toxicity class	Predicted LD50 (mg/kg)	Carcinogenicity	Hepato toxicity	Immuno toxicity	Nephro toxicity
1	Rosmarinic acid	4	1700	INACTIVE	ACTIVE	ACTIVE	INACTIVE
2	Ursolic acid	4	1190	INACTIVE	ACTIVE	ACTIVE	INACTIVE
3	Eugenol	4	1190	INACTIVE	ACTIVE	ACTIVE	INACTIVE
4	Caffeic acid	4	1190	INACTIVE	ACTIVE	ACTIVE	INACTIVE
5	Oleanolic acid	4	1700	INACTIVE	ACTIVE	ACTIVE	INACTIVE
6	Vicenin	4	1190	INACTIVE	ACTIVE	ACTIVE	INACTIVE
7	Voglibose	4	1190	INACTIVE	ACTIVE	ACTIVE	INACTIVE

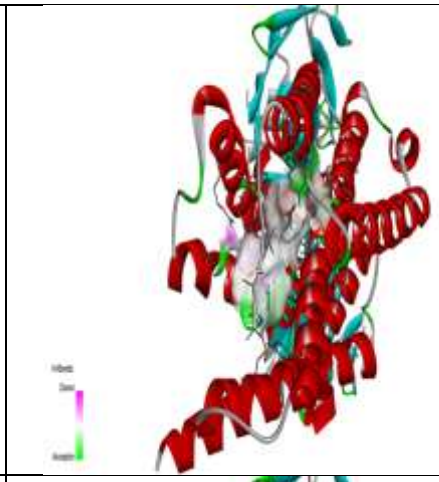
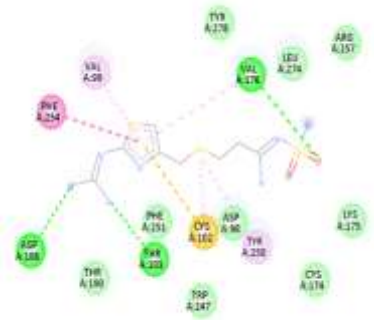
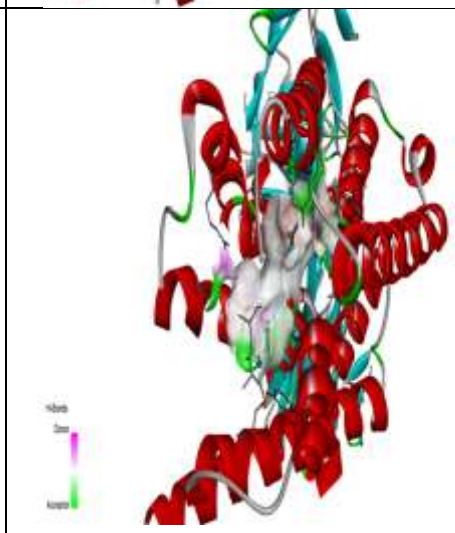
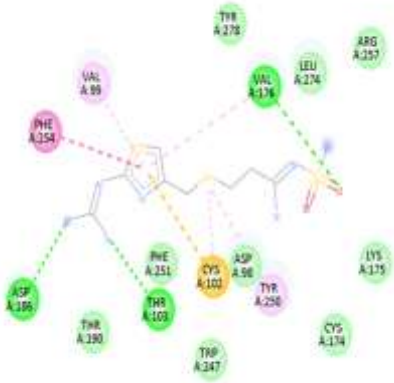
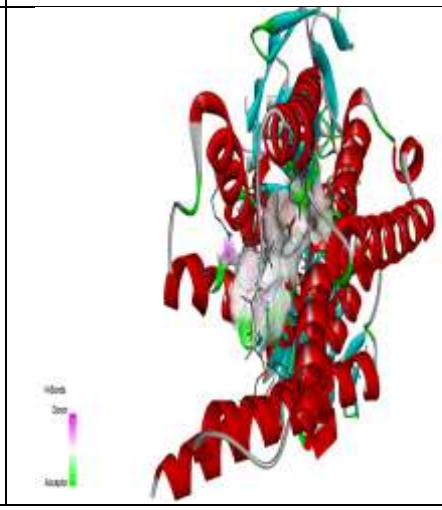
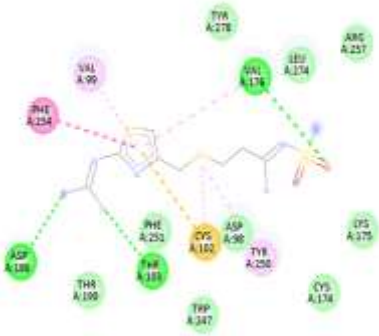
5. Binding Affinity

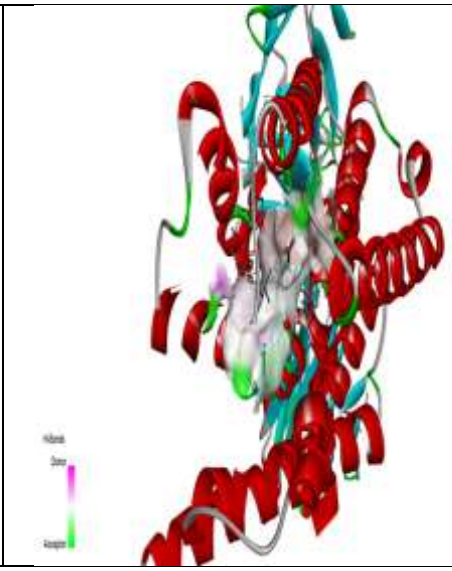
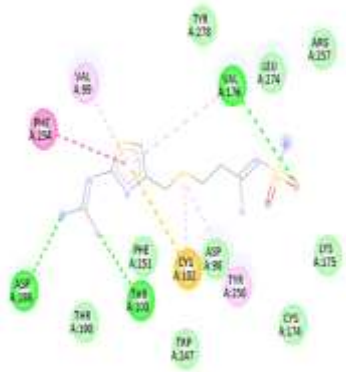
Table No.6. Binding affinity of Ligands

Sr. No	Ligands	Binding affinity
1	Rosmarinic acid	-6.8
2	Ursolic acid	-7.2
3	Eugenol	-
4	Caffeic acid	-4.8
5	Oleanolic acid	-5.7
6	Vicenin	-6.8
7	Voglibose	-5.5

6. 3D and 2D Structure of Ligands

Sr.No	LIGAND	3D STRUCTURE	2D STRUCTURE
1.	Caffeic acid		
2.	Olenolic acid		
3.	Vecinin		

4.	Rosmarinic acid		
5.	Eugenol		
6.	Ursolic acid		

7.	Voglibose		

6. CONCLUSION:

The Insilco studies of chemical constituents of plant Ocimum sanctum showed that Rosmarinic acid, Ursolic acid, Oleanolic acid, Vicenin have good binding affinity as compared to standard drug Voglibose but have same predicted toxicity class 4. Phytoconstituent Rosmarinic acid, Ursolic acid, Oleanolic acid, Vicenin show some have same ADME properties and Toxicity as Standard Drug Voglibose, but Phytoconstituent showing good binding affinity and this phytoconstituents are used further development of Anti-Diabetics Drug.

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