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Experimental And Computational Strategies for the Study of Diabetes: An Integrative Review

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Abstract: *Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia and is currently the third most significant global health threat, following cardiovascular diseases and cancer. Worldwide, the burden of diabetes continues to rise, with cases projected to reach 693 million by 2045. India is a major contributor to this global epidemic, with an estimated 62.4 million individuals affected by type 2 diabetes and 77 million with prediabetes, according to the ICMR–INDIAB study. Diabetes results from complex defects in insulin secretion, insulin action, or both, involving multiple organs, enzymes, and molecular pathways. Various in vivo models including streptozotocin (STZ), alloxan, dithizone, ferric nitrilotriacetate, insulin-antibody-induced diabetes, and gold-thioglucose models are widely used to mimic type 1 or type 2 diabetes. Complementary in vitro methods, such as α-amylase inhibitory assays, further aid in evaluating antidiabetic potential by assessing carbohydrate-digesting enzyme inhibition. This review summarizes the global significance, pathophysiology, classification, symptoms, diagnosis, prevention strategies, and current treatment options for diabetes mellitus. It also provides an extensive overview of the major in vivo and in vitro experimental models used to investigate antidiabetic activity, highlighting their mechanisms, procedures, and applicability in modern research.*

Keywords: Diabetes mellitus; Antidiabetic activity; Experimental animal models; Streptozotocin; In vitro assays; α-Amylase inhibition; Molecular docking; Medicinal plants

I. INTRODUCTION

According to the international diabetes federation diabetes ranks as the third most significant health threat globally following cardiovascular disease and cancer. The world health organization reports that as of 2015, approximately 415 million people worldwide had diabetes, with projection indicating a rise to around 693 million by 2045.(1) Diabetes mellitus is a chronic metabolic disorder marked by Persistent hyperglycemia classified as non communicable disease.(2) To the recently published Indian council of medical research India diabetes (ICMR – INDIAB) National study, approximately 62.4 million people in India have type 2 diabetes, and around 77 million people have pre diabetes.(3) The concept of developing an artificial pancreas, such as closed loop-control system to maintain normoglycemia, has been explored for type-1 diabetes mellitus (T1DM) since the 1970.(4)Individuals with irregularities in glucokinase, and enzyme crucial for glucose regulation, are often prone to developing conditions such as type 2 diabetes, hypoglycemia or hyperglycemia.(5) Diabetes profoundly affects multiple body systems, notably impairing the body's defence and immune system.(6) Diabetes mellitus (DM) has become a significant health concern in recent year, with its associated.(7) Globally , type 2 diabetes mellitus (T2DM) It's a leading cause of death, with over 70% of those affected residing in developing countries, and China having the largest number of cases with approximately 92.4 million .(8) Diabetes mellitus is a significant global health issue, recognized her as old lifestyle related syndrome that can lead to various complications, including retinopathy, neuropathy, and cardiovascular diseases.(9) Diabetes mellitus is a complicated disease because it can be caused by defects in many organs, proteins, and enzymes. (10) GLP-1 agonists are widely used for managing non-insulin-dependent diabetes mellitus (NIDDM) because they provide beneficial outcomes with a low risk of hyperglycemia compared with sulfonylureas (Garber, 2011).(11) Oral antidiabetic drugs may be useful for people who are allergic to insulin or do not use insulin injections.(12) Medicinal plants are a natural source of bioactive compounds with great therapeutic potential against several medical conditions, promoting overall health and well being. (13) Although

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combination therapies are available, they have limitations in their ability to manage the end stage of type 2 diabetes mellitus.[14]

II. MATERIAL AND METHODS

In vivo method

1. Streptozotocin Model of Diabetes Mellitus.

STZ damages DNA in pancreatic β-cells, leading to their destruction via necrosis. The procedure involves administering STZ (60mg/kg) intravenously to adult male Wistar rats, resulting in initial hyperglycemia, followed by hypoglycemia, and eventually persistent hyperglycemia.[15]

Procedure :

Modified STZ Model with Nicotinamide

A newer model combines STZ with nicotinamide (NAD) to induce stable, nonfasting hyperglycemia in adult rats. NAD protects against STZ's cytotoxic effects, resulting in a more balanced and stable hyperglycemic state. STZ (Streptozotocin) triggers a mechanism involving free radical generation, leading to oxidative stress. This oxidative stress causes a reduction in β-cells, resulting in insulin insufficiency and chronic hyperglycemia, ultimately leading to reduced β-cells. Simultaneously, oxidative stress causes neuronal injury via neuroinflammation, leading to neurodegeneration and cognitive dysfunction. [15]

2. Alloxan model of Diabetes Mellitus

Alloxan is a widely used diabetogenic agent that induces Type 1 diabetes in animals by selectively necrotizing pancreatic islet β-cells. This urea derivative is commonly used to create diabetes models in various animals, including rabbits, rats, mice, and dogs Alloxan is a widely used diabetogenic agent that induces Type 1 diabetes in animals by selectively necrotizing pancreatic islet β-cells.[15]

Procedure:

In White New Zealand rabbits (2.5-4 kg), Alloxan monohydrate (150 mg/kg) is infused via the marginal ear vein over 10 minutes, resulting in hyperglycemia and uricosuria in approximately 70% of animals.

In Wistar or Sprague Dawley rats (150-200 g), Alloxan monohydrate (100-175 mg/kg) is injected subcutaneously.

In male Beagle dogs (15-20 kg), Alloxan monohydrate (60 mg/kg) is administered intravenously, followed by 1000 ml of 5% glucose solution with 10 IU of regular insulin IV for one week, along with ad libitum canned food.[15]

3. Insulin Antibodies–Induced Diabetes

High-affinity insulin antibodies can bind circulating insulin and prevent it from acting on target tissues. As a result, affected animals develop postprandial hyperglycemia accompanied by elevated insulin levels.To experimentally induce this condition, bovine insulin is emulsified with complete Freund's adjuvant and injected subcutaneously into male guinea pigs at monthly intervals. Blood samples are later collected from these animals via cardiac puncture to obtain anti-insulin serum.[15]

4. Ferric Nitrilotriacetate Induction of Diabetes:

Parenteral administration of ferric nitrilotriacetate (Fe3+-NTA) in experimental animals for 60 days induces noticeable diabetic symptoms, including hyperglycemia, glycosuria, ketonemia, and ketonuria.[15]

Procedure :

Ferric nitrate is dissolved in 1.0 N HCl to prepare a Fe3+-NTA solution. This involves adding 162 ml of 0.1 M ferric nitrate solution to 100 ml of 0.08 M disodium nitrilotriacetate solution, with pH adjustment to 7.4 using sodium bicarbonate powder under magnetic stirring. The mixture is prepared fresh before use.

The study uses 224 inbred Wistar rats and 12 albino adult rabbits, divided into four major groups.

Group I (n=120) is further divided into four subgroups:

Group Ia receives escalating doses of Fe3+-NTA via intraperitoneal (i.p.) injections over 3 months (0.2-1.0 mg Fe/100g body weight), with a total iron dose of approximately 200 mg.

Group Ib (NTA controls) receives i.p. injections of disodium nitrilotriacetic acid (Na2NTA) at equivalent concentrations.

Group Ic receives i.p. injections of iron colloid (ferric hydroxide chondroitin sulfate colloid) at equivalent doses.

Group Id serves as untreated controls.

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Blood and urinary glucose and ketones are monitored weekly, with body weight measured twice weekly. Histological studies are conducted after sacrifice.

Group II (n=56) receives a single i.p. injection of Fe3+-NTA (1.0 mg Fe/100g body weight) to assess serum iron levels and total iron-binding capacity at various intervals.

Group III (n=24) receives daily Fe3+-NTA injections for 2 months, followed by weekly blood withdrawal (2 ml) for 4 weeks. Blood and urinary sugar are measured twice weekly, and histochemical investigations are performed after sacrifice.

Group IV (n=24) receives extended daily Fe3+-NTA injections until death, with histological observations conducted for cirrhotic changes. (15)

In vitro method

1. α-Amylase Inhibitory Activity

The α-amylase inhibitory activity of various extracts is commonly evaluated using modified protocols based on the method. In this assay, porcine pancreatic α-amylase is incubated with the test sample, and the enzymatic hydrolysis of starch is subsequently measured. The amount of reducing sugars produced, mainly maltose, is quantified using the 3,5-dinitrosalicylic acid (DNS) colorimetric method, with absorbance measured at around 690 nm.(16)

Procedure

1. Prepare starch substrate by dissolving 1 g of soluble starch in 100 mL of sodium phosphate buffer (0.1 M, pH 6.9).
2. Prepare alpha-amylase solution by diluting the enzyme to 50 U/mL in sodium phosphate buffer.
3. Prepare test compound solution by dissolving the compound in DMSO or water.

Assay Procedure

1. Add 50 µL of alpha-amylase solution to a microcentrifuge tube.
2. Add 50 µL of test compound solution (or solvent control) to the tube.
3. Incubate the mixture at 37°C for 10 minutes.
4. Add 100 µL of starch substrate to the tube.
5. Incubate the mixture at 37°C for 10-30 minutes (depending on the enzyme activity).
6. Stop the reaction by adding 200 µL of DNS reagent
7. Boil the mixture for 5 minutes to develop the color.
8. Cool the mixture to room temperature. Preparation of Reagents
9. Measure the absorbance at 540 nm using a spectrophotometer.(16)

2. Alpha glucosidase inhibitor assay :

The α-glucosidase inhibitory activity is assessed using a modified method based on Nishioka .The assay involves mixing 0.2 ml of 56 mM sucrose in 0.1 M potassium phosphate buffer (pH 7) with 0.1 ml of plant extract in 50% DMSO. After incubating at 37°C for 5 minutes, 0.2 ml of α-glucosidase solution (prepared from rat intestinal acetone powder) is added, and the mixture is further incubated for 30 minutes. The reaction is stopped with 0.75 ml of 2 M Tris-HCl buffer (pH 6.9), followed by centrifugation and filtration. (16)

Procedure

Preparation of Reagents

1. Prepare alpha-glucosidase solution by dissolving the enzyme in sodium phosphate buffer (0.1 M, pH 6.8) to a concentration of 1 U/mL.
2. Prepare PNPG solution by dissolving PNPG in sodium phosphate buffer (0.1 M, pH 6.8) to a concentration of 5 mM.
3. Prepare test compound solution by dissolving the compound in DMSO or water.

Assay Procedure

1. Add 50 µL of alpha-glucosidase solution to a microcentrifuge tube.
2. Add 50 µL of test compound solution (or solvent control) to the tube.
3. Incubate the mixture at 37°C for 10 minutes.

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4. Add 100 µL of PNPG solution to the tube.
5. Incubate the mixture at 37°C for 10-30 minutes (depending on the enzyme activity).
6. Stop the reaction by adding 100 µL of sodium carbonate (0.2 M).
7. Measure the absorbance at 405 nm using a spectrophotometer.[16]

3. Nitroblue tetrazolium assay :

The nitroblue tetrazolium (NBT) assay assesses respiratory burst activity in polymorphonuclear cells (PMNCs). Isolated PMNCs are resuspended in glucose-free RPMI (3 × 10^6 cells/ml) and distributed into 96-well plates with varying glucose concentrations. NBT and phorbol myristate acetate (PMA) are added, and the plates are incubated at 37°C followed by room temperature. [17]

Procedure

Preparation of NBT Solution

1. Dissolve NBT in PBS to a final concentration of 1 mg/mL.
2. Filter the solution through a 0.22 µm filter to remove any particulate matter.

Cell Preparation

Isolate cells (e.g., neutrophils, macrophages) and resuspend them in PBS at a concentration of 1-2 x 10^6 cells/mL.

NBT Assay

1. Add 100 µL of cell suspension to each well of a 96-well plate.
2. Add 100 µL of NBT solution to each well.
3. Add 10 µL of PMA or other stimulant to the wells (optional).
4. Incubate the plate at 37°C for 30-60 minutes.
5. Stop the reaction by adding 100 µL of methanol or other fixative.
6. Centrifuge the plate at 500 x g for 5 minutes.
7. Remove the supernatant and add 100 µL of DMSO to each well.
8. Incubate the plate at room temperature for 10-15 minutes.
9. Measure the absorbance at 540-560 nm using a microplate reader. [17]

III. HORMONE INDUCED DIABETES

3.1 Growth hormone induced diabetes

Growth hormone-induced diabetes can result in consequences like as kidney abnormalities. Recurrent injection of the hormone to cats and dogs can cause diabetes with all of its symptoms, including ketonemia and ketonuria. Chronic administration of the hormone can also cause damage to the pancreatic beta cells.[18]

3.2 Corticosteroid induced diabetes

Steroid diabetes is the name for the form of diabetes that can result from using corticosteroids to relieve inflammation. Prednisolone and dexamethasone are the two glucocorticoids that induce steroid diabetes most commonly. Glucocorticoids inhibit the effects of insulin and promote gluconeogenesis, particularly in the liver. Thisleadsto an overall increase in the amount of glucose produced by the liver and the development of insulin resistance, hyperglycemia, and hyperlipidemia. [18]

In silico methods :

1.Molecular Docking Analysis :

We performed molecular docking studies using AutoDock (v4.0) and PatchDock to investigate the interactions between the native and mutant anaplastic. The structure generated from SMILE strings and energy-minimized. Auto dock used with the genetic algorithm (LGA) for docking experiments, employing the following parameters: 30 independent runs, population size of 150, 25,000,000 energy evaluations, 27,000 generations, mutation rate of 0.02, and crossover rate of 0.8. [19]

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Procedure

1. Protein Preparation: The 3D structure of the protein is retrieved from databases such as Protein Data Bank (PDB) or predicted using homology modeling.
2. Ligand Preparation: The 3D structure of the ligand is generated using software such as ChemDraw or OpenBabel.
3. Docking Protocol: A docking protocol is defined, which includes the scoring function, search algorithm, and grid size.
4. Docking Simulation: The ligand is docked into the protein binding site using the defined protocol.
5. Scoring and Ranking: The docked poses are scored and ranked based on their binding affinity.
6. Analysis and Visualization: The top-ranked poses are analyzed and visualized using software such as PyMOL or Chimera. [19]

2. Molecular dynamics simulation :

Molecular dynamics simulations of the complex using the GROMACS Package with the force field. The lowest binding energy conformation generated by AutoDock used as the initial conformation for MD simulation. Topology parameters for the proteins were created using the Gromacs program, while the Dundee prodrug server used to build topology parameters for crizotinib. The complex solvated in an octahedral box of simple point charge (SPC) water molecules, and eight Na+ counter-ions were added to ensure overall charge neutrality. The native and mutant complexes underwent energy minimization using steepest descent (10,000 steps) followed by conjugate gradient (10,000 steps).[19]

Procedure

1. System Preparation: The molecular system is prepared, including the protein, ligand, and solvent molecules.
2. Energy Minimization: The energy of the system is minimized using techniques such as steepest descent or conjugate gradient.
3. Equilibration: The system is equilibrated to a stable temperature and pressure using techniques such as NVT or NPT ensemble.
4. Production Run: The MD simulation is run for a specified time period, typically in the range of nanoseconds to microseconds.
5. Analysis: The trajectory of the simulation is analyzed to extract relevant information, such as protein-ligand interactions, conformational changes, and thermodynamic properties.[19]

IV. QSAR MODEL

4.1 Target Protein Preparation and Docking Procedure:

The target protein preparation and docking procedure involves retrieving the crystallographic structure of protein from the RCSB database. The monomeric protein (chain A) is prepared using Schrödinger's protein preparation wizard. A grid coordinate is generated at the binding domain of the co-crystallized ligand using the receptor grid generation tool. The prepared compounds are virtually screened against the target's binding site, and site-directed docking is performed using an extra precision filtering procedure to estimate binding affinity.[20]

Procedure

Target Protein Preparation

1. Protein Structure Retrieval: Retrieve the protein structure from the other databases.
2. Protein Structure Cleaning: Remove any unwanted molecules, such as water, ions, or ligands, from the protein structure.
3. Protein Structure Optimization: Optimize the protein structure using energy minimization techniques, such as steepest descent or conjugate gradient.
4. Protonation State Assignment: Assign protonation states to the protein residues, taking into account the pH and pKa values.
5. Ligand Binding Site Identification: Identify the ligand binding site on the protein surface.

Docking Procedure

1. Ligand Preparation: Prepare the ligand structure, including protonation state assignment and energy minimization.

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2. Docking Grid Generation: Generate a docking grid around the ligand binding site, defining the search space for the ligand.
3. Docking Algorithm Selection: Select a docking algorithm, such as genetic algorithm or simulated annealing.
4. Docking Simulation Perform the docking simulation, using the selected algorithm and docking grid.
5. Scoring and Ranking: Score and rank the docked poses based on their binding affinity and other criteria.[20]

4.2 Fitness Score Estimation via Pharmacophore Modeling:

A pharmacophore hypothesis is generated using the receptor-ligand complex of protein with its co-crystallized ligand via Maestro suite. The hypothesis is used to screen and analyze the bioactive compounds. Fitness scores of the compounds are evaluated using the Phase screen module, assessing their alignment with the pharmacophore model.[20]

Procedure

1. Target Protein Selection: Select a target protein with known structure and function.
2. Ligand Selection: Select a set of known active ligands that bind to the target protein.
3. Pharmacophore Generation: Generate a pharmacophore model using the selected ligands.
4. Pharmacophore Refinement: Refine the pharmacophore model using molecular superposition and feature extraction techniques.[20]

4.3 PIC50 Estimation via QSAR Model:

The process of estimating PIC50 via a QSAR model involves retrieving a dataset of protein from the ChEMBL database using the α-amylase FASTA sequence. The dataset is converted to SDF format using DataWarrior and imported into Maestro software for preparation. The macromodel minimization tool is used to prepare the molecules, and their PIC50 values are utilized to develop a QSAR model.[20]

procedure:

Data Collection :

Gather compounds with known IC50 values (same assay preferred). Convert IC50 to pIC50: _pIC50 = -$\log_{10}$(IC50 in M)_. Ensure a diverse chemical space.

Molecular Descriptor Calculation :

Use tools like Dragon, RDKit, or PaDEL-Descriptor. Calculate:

Physicochemical: logP, H-bonds, molecular weight.

Topological: connectivity, shape.

Electronic: charges, polarizability.

Remove redundant/correlated descriptors.

Data Splitting

Split into training (70-80%) for model building and test (20-30%)for validation. Match chemical diversity.

Model Building

Methods: MLR (simple), PLS (handles collinearity), Machine Learning(nonlinear). Use R, Python (scikit-learn), or QSAR tools.

Model Validation

Internal: Cross-validation (e.g., k-fold), check R^2, Q^2.

External:Predict test set pIC50. Evaluate R^2_test, RMSE. Watch for overfitting.

Applicability Domain

Define domain (e.g., leverage, PCA). Ensure predictions are reliable.

Prediction

Input new compound's descriptors. Get predicted pIC50 ± uncertainty. [20]

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V. TARGET-PEPTIDE DOCKING

5.1 Preparation of the structure of the targets

Procedure

Step 1: Protein Structure Retrieval

1. Retrieve the protein structure: Retrieve the protein structure from the other databases.
2. Check the structure quality: Check the structure quality, resolution, and completeness.

Step 2: Protein Structure Cleaning

1. Remove unwanted molecules: Remove unwanted molecules, such as water, ions, or ligands, from the protein structure.
2. Remove missing atoms: Remove missing atoms or residues from the protein structure.
3. Fix structural errors : Fix structural errors, such as incorrect bond lengths or angles.

Step 3: Protein Structure Optimization

1. Energy minimization : Perform energy minimization to optimize the protein structure.
2. Molecular dynamics simulation : Perform molecular dynamics simulation to optimize the protein structure.

Step 4: Protonation State Assignment

1. Assign protonation states : Assign protonation states to the protein residues, taking into account the pH and pKa values.
2. Check protonation states : Check the protonation states of the protein residues.

Step 5: Ligand Binding Site Identification

1. Identify the ligand binding site: Identify the ligand binding site on the protein surface.
2. Define the binding site : Define the binding site using a set of residuce or grid.[21]

5.2 Preparation of Peptide Structure and Docking

Procedure

Peptide Structure Generation

1. Sequence Retrieval : Retrieve the amino acid sequence of the peptide.
2. SMILES String Generation: Convert the peptide sequence into a SMILES string format using tools like PepSMI.
3. 3D Structure Generation: Convert the SMILES string into a 3D structure using tools like DataWarrior.

Peptide Structure Optimization

1. Protonation State Assignment : Assign protonation states to the peptide residues, taking into account the pH and pKa values.
2. Energy Minimization : Perform energy minimization to optimize the peptide structure.
3. Molecular Dynamics Simulation : Perform molecular dynamics simulation to optimize the peptide structure.[21]

5.3 Characterisation of Target-Peptide Interactions

We attempted to access information on the characterisation of interactions between peptides and protein targets using the Protein-Ligand Interaction Profiler (PLIP) web server.[21]

Procedure

Molecular Docking

Steps:

1. Prepare the protein and peptide structures.
2. Define the binding site.
3. Perform docking simulation.
4. Analyze the results.

2. Molecular Dynamics Simulation

Steps:

1. Prepare the protein-peptide complex structure.
2. Define the simulation parameters.
3. Run the simulation.
4. Analyze the results.

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3. Protein-Ligand Interaction Profiler (PLIP)

Steps:

1. Upload the protein-peptide complex structure.
2. Select the interaction types to analyze.
3. Run the analysis.
4. Visualize the results.[21]

Discussion

Diabetes mellitus, a chronic metabolic disorder marked by persistent hyperglycemia, poses a significant global health challenge, with the International Diabetes Federation identifying it as the third most pressing health issue after cardiovascular diseases and cancer. The global prevalence is staggering, with over 415 million people affected, a number projected to rise to 693 million by 2045. In India alone, approximately 62.4 million people are living with type 2 diabetes (T2DM), a condition driven largely by lifestyle factors like obesity and physical inactivity. The complexity of diabetes, with its impact on multiple organs and systems, has spurred ongoing research into more effective treatments, including the development of the artificial pancreas and GLP-1 agonists, which aim to regulate blood glucose levels. In diabetes research, in vivo methods provide insight into whole-body glucose homeostasis, insulin sensitivity, and long-term complications using diabetic animal models. In vitro methods allow detailed investigation of cellular mechanisms such as insulin secretion, glucose uptake, and enzyme inhibition under controlled conditions. In silico approaches complement these studies by predicting drug–target interactions, optimizing lead compounds, and reducing experimental cost and time. The combined use of in vivo, in vitro, and in silico methods offers a more reliable and efficient strategy for understanding diabetes pathophysiology and developing novel antidiabetic agents.

VI. CONCLUSION

Diabetes mellitus is a pervasive and chronic metabolic disorder that poses significant global health challenges, with escalating prevalence rates, particularly in developing nations like India. It encompasses a range of types, including type 1, type 2, gestational, and others, each characterized by distinct pathophysiological mechanisms that contribute to heightened morbidity and mortality. Notwithstanding advancements in treatment modalities, including oral antidiabetic agents and insulin therapy, effective diabetes management remains elusive due to complications stemming from metabolic dysregulation, oxidative stress, and inflammation. Animal models, such as streptozotocin- or alloxan-induced models, have been instrumental in elucidating the molecular underpinnings of the disease, although the complexity of diabetes necessitates a multifaceted approach to treatment. Lifestyle interventions, comprising healthy dietary habits, regular physical activity, and stress management, remain essential preventive strategies. in vivo, in vitro, and in silico methods play a complementary role in diabetes research. In vivo models such as streptozotocin- or alloxan-induced diabetic animals help evaluate glucose regulation and antidiabetic efficacy, in vitro studies using pancreatic β-cells, adipocytes, or enzyme inhibition assays (α-amylase, α-glucosidase) clarify cellular mechanisms, and in silico approaches aid in predicting drug–target interactions, efficacy, and safety. Together, these methods enhance understanding of diabetes and support the development of effective antidiabetic therapies.

REFERENCES

[1]. Luo W, Deng J, He J, Yin L, You R, Zhang L, et al. Integration of molecular docking, molecular dynamics and network pharmacology to explore the multi-target pharmacology of fenugreek against diabetes. J Cell Mol Med. 2023;27(11):2795– 2811. Doi:10.1111/jcmm.17787.

[2]. Li MH, Jin MH, Li W. Exploring the mechanism of active components from ginseng to manage diabetes mellitus based on network pharmacology and molecular docking. Sci Rep. 2023;13:793. Doi:10.1038/s41598-023-27710-w.

[3]. Kaushik P, Khokra SL, Rana AC, Kaushik D. Pharmacophore modeling and molecular docking studies on Pinus roxburghii as a target for diabetes mellitus. Biomed Res Int.2014;2014:903246. Doi:10.1155/2014/903246

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[4]. Magni L, Raimondo DM, Bossi L, Dalla Man C, De Nicolao G, Kovatchev B, et al. Model Predictive control of type 1 diabetes: an in silico trial. J Diabetes Sci Technol. 2007;1(6):804–812. Doi:10.1177/193229680700100604

[5]. Balamurugan R, Stalin A, Ignacimuthu S. Molecular docking of γ-sitosterol with some targets related to diabetes. Eur J Med Chem. 2011;46(11):5395–5401. Doi:10.1016/j.ejmech.2011.10.007 6. Daoud AK, Tayyar MA, Fouda IM, Abu Harfeil N. Effects of diabetes mellitus vs. in vitro hyperglycemia on select immune cell functions. Immunol Invest. 2009;38(1):36–41. Doi:10.1080/15476910802604564

[6]. Kahksha, Alam O, Al-Keridis LA, Khan J, Naaz S, Alam A, Ashraf SA, Alshammari N, Adnan M, Beg MA. Evaluation of antidiabetic effect of luteolin in STZ induced diabetic rats: molecular docking, molecular dynamics, in vitro and in vivo studies. J Funct Biomater. 2023;14(3):126. Doi:10.3390/jfb14030126

[7]. Rampogu S, Lemuel MR. Network based approach in the establishment of the relationship between type 2 diabetes mellitus and its complications at the molecular level coupled with molecular docking mechanism. J Diabetes Res. 2016;2016:6068437. doi:10.1155/2016/6068437.

[8]. Hayat S, Ullah H, Rahim F, Ullah I, Taha M, Iqbal N, Khan F, Khan MS, Shah SAA, Wadood A, Sajid M, Abdalla AN. Synthesis, biological evaluation and molecular docking study of benzimidazole derivatives as α-glucosidase inhibitors and anti-diabetes candidates. J Mol Struct. 2022;1263:134774. doi:10.1016/j.molstruc.2022.134774.

[9]. Arif R, Ahmad S, Mustafa G, Mahrosh HS, Ali M, Tahir ul Qamar M, Dar HR. Molecular docking and simulation studies of antidiabetic agents devised from hypoglycemic polypeptide-P of Momordica charantia. Biomed Res Int. 2021;2021:5561129. doi:10.1155/2021/5561129.

[10]. Ahmed D, Khan MI, Kaithwas G, Roy S, Gautam S, Singh M, Devi U, Yadav R, Rawat J, Saraf S. Molecular docking analysis and antidiabetic activity of rifabutin against STZ-NA induced diabetes in albino Wistar rats. Beni-Suef Univ J Basic Appl Sci. 2017;6(4):326-332. Doi:10.1016/j.bjbas.2017.04.010.

[11]. Gharge S, Kagawad P, Palled MS, Maste MM, Suryawanshi SS. In-silico molecular docking in screening of anti-diabetic therapeutics from medicinal plants. Int J Ayurvedic Med. 2021;12(2):190-198.

[12]. Ajayi OS, Fakola EG, Olubiyo FF, Balogun OS, Olawuni IJ, Kelani TO. Antioxidant, antidiabetic and molecular docking studies of D-pinitol isolated from Cleistopholis patens (Benth) leaf extract. Discover Chemistry. 2025;2:129. Doi:10.1007/s44371-025-00200-4.

[13]. Ilyas U, Nazir B, Altaf R, Muhammad SA, Zafar H, Paiva-Santos AC, Abbas M, Duan Y. Investigation of anti-diabetic potential and molecular simulation studies of dihydropyrimidinone derivatives. Front Endocrinol (Lausanne). 2022;13:1022623. Doi:10.3389/fendo.2022.1022623.

[14]. Dewangan H, Tiwari RK, Sharma V, Shukla SS, Satapathy T, Pandey R. Past and future of in-vitro and in-vivo animal models for diabetes: a review. Indian J Pharm Educ Res. 2017;51(4s):S626–S634. doi:10.5530/ijper.51.4s.79.

[15]. Boaduo NKK, Katerere D, Eloff JN, Naidoo V. Evaluation of six plant species used traditionally in the treatment and control of diabetes mellitus in South Africa using in vitro methods. Pharm Biol. 2014;52(6):756–761. doi:10.3109/13880209.2013.869828

[16]. Daoud AK, Tayyar MA, Fouda IM, Abu Harfeil N. Effects of diabetes mellitus vs. in vitro hyperglycemia on select immune cell functions. Immunotoxicol. 2009;31(1):36–41. doi:10.1080/15476910802604564

[17]. Tripathi V, Verma J. Different models used to induce diabetes: a comprehensivereview. Int J Pharm Pharm Sci. 2014;6(6):29-32.

[18]. Doss CGP, Chakraborty C, Chen L, Zhu H. Integrating in silico prediction methods, molecular docking, and molecular dynamics simulation to predict the impact of ALK missense mutations in structural perspective. BioMed Res Int. 2014;2014:895831. doi:10.1155/2014/895831

[19]. Omoboyowa DA, Aribigbola TC, Akinsulure ST, Bodun DS, Olugbogi EA, Oni E. In vitro and in silico anti-diabetes mechanism of phytochemicals from Curculigo pilosa and its pharmacokinetic profiling via α-amylase inhibition. Adv Mod Lett Med. 2025;100064. doi:10.1016/j.amolm.2025.100064

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[20]. Teixeira CSS, Villa C, Sousa SF, Costa J, Ferreira IMPLVO, Mafra I. An in silico approach to unveil peptides from Acheta domesticus with potential bioactivity against hypertension, diabetes, cardiac and pulmonary fibrosis