

**Abstract**

One of the most widely spreading diseases due to several lifestyle problems in the 21st century is diabetes mellitus. The management of diabetes mellitus is very important and essential. Plants are natural reservoir of many medicinal value added components help to overcome many chronic disorders including diabetes mellitus. Herbal drugs are prescribed in treatment of diabetes mellitus due to their good effectiveness, fewer side effects in clinical experience and relatively low costs. Screening of antidiabetic therapeutics is very important and essential for effective management of diabetes mellitus. Many researchers have worked on extraction, isolation, characterization of extracts and bioactive fractions from medicinal plant also they have established profile and data of interaction of active components against various targets and enzymes of diabetes mellitus using *In-silico* molecular docking tools. Molecular docking is an important computational tool to predict the plausible interactions between the drug and protein in a non-covalent fashion. Extensive in silico docking procedures have been carried out to examine whether the compound is a good ligand with diabetic targets. In the present review article we have thoroughly screened research articles published in various scientific, indexed, national and international journals on *In-silico* molecular docking based screening of Anti-Diabetic potentials and therapeutics from medicinal plant and extensively presented.

**Key Words:** Diabetes Mellitus, Diabetic Targets, Herbal Drugs, Molecular Docking, Protein.

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**Introduction**

One of the most widely spreading diseases due to several lifestyle problems in the 21st century is diabetes mellitus (DM). This disease is generally classified by insulin-dependent or type 1 DM, which is mainly initiated by destruction of the insulin producing pancreatic β-cells, and nondependent insulin or type 2 DM, and this is triggered by lifestyle-related obesity or other exogenous components involve in it. People with type 2 diabetes are not dependent on exogenous insulin and People with type 1 diabetes need to take insulin injection for survival. In the treatment of diabetes, the drug consumption is a complementary treatment besides from diet. Oral antidiabetic drugs may be useful for people who are allergic to insulin or do not use insulin injection. And the use of these drugs in the long term has lots of disadvantages, which mainly causing increasing the risk of heart attack and acute kidney toxicity. Therefore, many efforts to develop traditional medicine for the treatment of diabetes are mounting (1).

Plants are natural reservoir of many medicinal value added components helps to overcome many chronic disorders. Hence herbal medicines are considered to be an excellent remedy for diseases like cancer, diabetes, liver diseases and arthritis. The bioactive compounds of medicinal plants like *Ruellia tuberosa*, *Grewia hirsuta*, *Albizia lebbeck benth.*, *Phyllanthus emblica*, *Piper longum* linn etc are used as anti-diabetic, chemotherapeutic, anti-inflammatory, anti-arthritic agents where no satisfactory cure is present in modern medicines. The bioactive compounds of medicinal plants are used as chemotherapeutic, anti-diabetic, anti-arthritic agents, anti-inflammatory where no satisfactory cure is present in modern medicines. Screening of antidiabetic therapeutics is very important and essential for effective management of DM. Many researchers have worked on extraction, isolation, characterization of extracts and bioactive fractions from medicinal plant also they have established profile and data of interaction of active components against various targets and enzymes of DM using *In-silico* molecular docking tools.

**Molecular docking is an important computational tool to predict the possible interactions between the drug and protein in a non-covalent fashion. Extensive in silico docking procedures have been carried out to examine whether the compound is a good ligand with diabetic targets such as Aldose reductase, Peroxisome proliferatoractivated receptor-gamma, Glycogen synthase kinase-3, Pyruvate dehydrogenase**

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kinase isoforms 2, Glucokinase, 11β-Hydroxysteroid dehydrogenase, Glutamine, fructose6-phosphate, amidotransferase (2). Molecular docking was performed in the form of flexible docking for the prediction of ligand efficiency, binding affinity and the inhibitory constant. All of the ligands were docked with the target active site. Active compounds will only have positioning that avoids penalties and receives favourable scores for accurate hydrophobic contacts between the protein and ligand (3).

Materials and Methods

Collection of Data

The relevant information and literature is reviewed, referred and collected from various databases and journal sites. Various databases like Pubmed, Scopus, Web of Science and other related plant and medicinal plant research sites were used for searching the information and articles. Published work and literature mainly related to “In-Silico Molecular Docking in Screening of Anti-Diabetic Therapeutics from Medicinal Plants” were collected and downloaded from journal related to medicinal plants, herbal medicines and Ayurvedic sciences and other journal related to traditional systems medicine. Published research works on molecular docking based screening of anti-diabetic potentials of plant and extracts were selected from net resources and reviewed. In the present review article, we have thoroughly screened research articles published in various scientific, indexed, national and international journals on In-silico molecular docking based screening of Anti-Diabetic potentials and therapeutics from medicinal plant and extensively reviewed.

Various research articles, data, and reports published by scientist on docking based identification and study of interaction of targets and ligands from medicinal plants were presented as follows:

Anna Safitri et al., have reported antidiabetic activity by In-Silico method by using aqueous extracts of Ruellia tuberosa L by using molecular docking using phenolic compound and the interaction between betaine, didzein and hispidulin in docking with human pancreatic α-amylase shows different binding by hydrogen and hydrophobic bond which shows good interactions and which inhibits α-amylase protein and shows antidiabetic activity (1).

Abirami Natarajan et al., have reported by methanolic extract of Grewia hirsuta by using molecular docking studies of ligand (4Z,12Z)-cyclopentadeca-4,12-diene and docking with several different target proteins shows that it has good inhibition property, which docks well with various targets related to antidiabetic activity (2).

Prabhu Srinivasan et al., have reported which shows antidiabetic activity of quercetin by methanolic extract from Phyllanthus emblica L fruitbyin-silico molecular docking studies which shows better docking score to glucogen phosphorylase with quercetin than with gallic acid and different concentration of quercetin shows antihyperglycemic effect and potent defense mechanism in STZ (Streptozotocin) induces antidiabetic activity (3).

Sodik Numanov et al., have reported antidiabetic activity and chemical composition of Geranium collinum root extract by molecular docking analysis suggests polyphenolic compounds such as corilagin, categin and caffeic acid inhibit PTP-1B and β-sitosterol-30-β-D-gluco-pyranoside inhibits α-glucosidase shows antidiabetic activity (4).

Danish Ahmed et al., have reported antidiabetic activity by molecular docking studies of some flavonoids from ethanolic extract of Albizia Lebbeck benth bark that inhibit α-glucosidase and alpha-amylyase enzyme targets to reduce glucose level and molecular docking study says binding affinity and inhibition of α-glucosidase and α-amylyase enzyme with DPPH which shows good binding interaction shows antidiabetic activity (5).

Quy Trinch et al., have reported antidiabetic activity of bioactive compounds in Euphorbia hirta L using molecular docking showing that flavonoid and terpenes families including cyanadin,3,5-O-diglucose myricitin, perlargonium-3-5-diglucose, quercetin, rectin, α-amynie, β-amynie and taraxerol have high binding affinity with a specific enzyme receptor and shows antidiabetic activity (6).

Laura Guasch et al., have reported antidiabetic activity by PPAR-γ (Potential peroxisome proliferators activated receptor gamma) partial agonist of natural origin by initial set of 29,779 natural products have proticated PPAR-γ partial agonist 12 molecules from 11 extracts known to have antidiabetic activity (7).

Juan Jose Ramirez Espinosa et al., have reported antidiabetic activity by pentacyclic acid triterpenoid’s role of PTP-1B by In-Silicomethod and related triterpinic acid, anolic, moronic, morolic acid which shows extensive hydrogen bond network with carboxyl group and Vander Waals interactions stabilizes the protein-ligand complex which shows antidiabetic activity (8).

Bikash Thakuria et al., have reported bioinformatics-based investigation to screen and analyze the bioactivity of Piper longum linn, which shows antidiabetic activity and the ligands of piperine, retrofractamide A, piper-longumine indicated great docking with piperine shows -8.69kcal/mol restricting vitality of 0.429μm hindrance which has greatest potential to be decent inhibitor against focused receptors which shows antidiabetic activity (9).

Aristeidis Pritsas et al., have reported vularisation of stachysetin from cultivated Stachys ira Griseb which shows antidiabetic agent, in silico screening against 17 proteins implicated in diabetes as also ligand-based similarity metrics against established antidiabetic activity drug and stachysetin shows binding profile to major drug carrier plasma protein serum albumin was explored along with its properties shows antidiabetic activity (10).

Zoy I Noor et al., have reported in-silico molecular docking stimulations with α-amylase and α-lipase enzyme of polar and non-polar extracts of leaves and flowers Ocimum basilicum and In-Silicostudy.
linalool and estragole to have considerable porcine pancreatic α-amylase (PPA) and porcine pancreatic lipase (PPL) binding potential and which further investigated through molecular dynamics and binding free energy calculations which shows best antidiabetic activity (11).

Abhijit Pathak et al., have reported in silico molecular docking analysis of isolated compounds of *Ocimum sanctum* against antidiabetic activity and a wide range of docking score found during molecular docking by maestro v 10.1 (Schrodinger) and among them carvacrol had lowest docking score against α-amylase enzymes and glucokinase which is -50521kJ/mol and -7.322kJ/mol and this is concluded less docking score compound will be more potent and shows antidiabetic activity (12).

T. Hoang Nguyen Vo et al., have reported in-silico molecular docking analysis from *Euphorbia thymifolia* it has 7 compounds were chosen to due high absolute value of binding energy to all four receptors (>8 kcal/mol) known as β-amyrine,toraxerol,1-O-galloyl-β-D-glucose ,corilagin,cosmossin,quercetin-3-galactoside and quercetin ,tannins, polyphenols and flavonoid family had high binding affinity to all receptors beside that , the binding affinity of two of terpenoid compounds has good prospect for treatment of type-2 diabetes mellitus (13).

Jasmine R et al., have reported antidiabetic activity in Streptozotocin (STZ) diabetic rats by in-silico method of molecular screening method which shows antidiabetic activity against target proteins like PPAR-γ which plays a role in protecting β-cells from damage was undertaken and docking analysis in active site of 2PRG was performed by Schrodinger program and it shows good binding interactions of ligands with targets at low energy level from terpenoid from *Elephantopus scaber L*, it increases insulin secretion from regenerated pancreatic β cells which is potent antidiabetic activity (14).

G. Mahendran et al., have reported in-silico antidiabetic activity isolated from *Swertia corymbose* which having 1,2,8-trihydroxy-6-methoxy xanthon (ligand 1) and 1,2-dihydroxy-6-methoxy xanthone-8-O-β-D-xylo pyranosyl (ligand 2) isolated from *Swertia corymbose*which shows antidiabetic activity by molecular docking studies by STZ(Streptozotocin) induced diabetic rats and ligand 1 and 2 and glibenamide with various diabetic docked with glucokinase , fructose-1,6-biphosphatase 1 with sulfonl urea receptor shows good binding activity towards antidiabetic activity (15).

Md. Nazmul Prottoy et al., have reported by molecular docking pharmacological property analysis of an antidiabetic activity of some medicinal plants of Bangladesh against type 2 diabetes by *In-Silico* computational approach and some of them are Aegeline from *Aegle maemelos*, gallic acid from *Terminalia belirica*, quercetin from *Psidium guajava* and mangiferin from *Mangifera indica* have antidiabetic activity among them quercetin have greatest source of antidiabetic activity (16).

Ranjit D et al., have reported *In-Silico* antidiabetic activity of bioactive compound in *Ipomoea mauritiana* juck which shows molecular interactions by using Argus lab docking software4.0.1 among this taraxerol shown maximum inhibition for 3G9E protein both shows antidiabetic activity (17).

Pradeep Paudel et al., have reported antidiabetic activity by *In-Silico* molecular docking study of 2.3.6-tribromo-4.5-dihydroxybenzyl derivatives from marine algae *Symphyododadua lattiuscula* through PTP1B (tyrosine phosphate 1 B) down regulation and α-glucosidase inhibition which shows antidiabetic activity (18).

Yue Chen et al., have reported by *In-Silico* molecular docking studies which shows antidiabetic activity from Ellagitannins isolated compound from unripe fruit *Kabus chingii hu* which shows molecular docking results revealed that Ching tannin A interacted with enzymes mainly by H-bond and was bound in allosteric site which shows good interaction and act as antidiabetic activity (19).

Jirawat Riyaphan et al., have reported hypoglycemic efficacy of *In-Silico* molecular docking selected natural compounds against α-glucosidase and α-amylase via molecular docking and enzymatic measurement on CaCo-2 cell and act as antidiabetic agent (20).

Rangachari Balamurugan et al., have reported γ-sitosterol isolated from *Lippia nodiflora* was taken as ligand for molecular docking and the targets like glucokinase, fructose-1,6-biphosphatase 1, by human multidrug resistance protein 1 and Cytochrome P 450 by autodock tool v 4.2 and APT V 1.5.4 program and γ-sitosterol which deals well with various targets related to diabetes mellitus (21).

Priyanka Sharma et al., have reported in-silico screening of potential antidiabetic activity from *Phyllanthus emblica*against the type-2 diabetes and docking score and pharmacophore studies found that ellagic acid, estradiol, sesamine, kaempferol, zeatin, quercetin and leucodelphinidin are potential antidiabetic activity (22).

Hyun Ah Jung et al., have reported molecular docking studies of an antidiabetic complication inhibitor such as fecosterol from edible brown algae *Eisenia bicyclis* and *Ecklonia stolonifera* which shows evaluating ability of this compound to inhibit rat lense aldose reductace (RLAR), human recombinant aldose reductase (HRAR), protein tyrosine phosphatase (PTP1B) and α-glucosidase which shows binding energy (-8.2kcal/mol) for RLAR and (-8.5kcal/mol) for HRAR showing molecular docking analysis of isolated compounds of *Phyllanthus emblica*  which shows antidiabetic activity (23).

Andrea S.P. Pereira et al., have reported antidiabetic activity of some common herbs and species by providing them by some *In-Silico*virtual screening method by in-silico method by using antidiabetic drug targets such as achillin B from yarrow, asparasaponin I from fenugreek, bisdemothoxy curcumin from turmeric , carlinoside from lemon grass with major protein targets like dipeptidyl-peptidase-4(DPP4), intestinal maltase-glucamylase liver receptor alpha ,protein tyrosine phosphatase non-receptor type.
interaction which indicates antidiabetic potential of common herbs and species (24).

Mingzhu Jiang et al., have reported In-Silico molecular docking study with α-glucosidase inhibitory peptides from Soybean protein hydrolysat which significantly reduces levels of fasting blood glucose in mice and this confirms that α-glucosidase inhibitory peptide may have hypoglycemic efficacy (25).

Nahid Ghaedi et al., have reported antidiabetic activity of alcoholic extract of leaf and stem of Levisticum officinaleae of an implication for α-amylase inhibitory activity of extract ingredient by molecular docking method that which shows antihyperglycemic effect of it among them luteolin, quercetin, rosmarinic, caffeic and hexanoic acids have greatest α-amylase inhibition activity (26).

Sarfraz Ahmed et al., have reported In-Silicomolecular docking studies on miquelianin isolated from aerial part of Euphoria schimperi c exhibited significant results for antidiabetic potential and miquelianin which significant α-amylase and α-glucosidase inhibitory activity which shows antidiabetic activity (27).

Vineet Mehta et al., have reported antidiabetic activity of hydroalcoholic extract from Ocimumcanctum which says greatly inhibited α-glucosidase enzyme but failed to inhibit α-amylase activity and docking studies predicted that rosmarinic acid, stigmasterol, linalool, aesculin may be responsible for antidiabetic activity possessed by plant through their interaction with insulin receptor (28).

P. Rajkumar et al., have reported antidiabetic activity compounds from the flowers of Cassiaauriculata by structure based molecular docking studies, which says that docking results showed best glide energy, docking score H-bonding interactions compared with molecular targets and has potential to prevent or treat type-2 diabetessmellitus (29).

Farhat Saghir et al., have reported In-Silico molecular docking screening studies from hexane extract of Pongamia pinnata flower which shows antidiabetic activity and molecular docking studies which indicates high binding energy scored with antidiabetic targets as compared to standard drug acarbose and results shows isolated compound 1-(4-methoxy-7-phenyl-5H-furo [3,2,9][1] benzopyran-5-one) has antidiabetic activity (30).

Jae Sue Choi et al., have reported antidiabetic activity of protein tyrosine phosphatase 1B inhibitor activity of alkaloids from Rhizoma Coptidis by molecular docking studies which conclude that alkaloids of Rhizoma coptidis (berberine, magnololrine, coptisine, epiberberine) exhibited remarkable inhibitory activities against PTP1B which has good binding affinity and docking score against PTP1B which shows antidiabetic activity (31).

Sudhanshu Kumar Bharti et al., have reported antidiabetic activity of fruto and isomal to oligosaccharides by In-Silicos studies by docking were performed by GLIDE program for each fos (Frutooligosaccharides) and IMO’S (Isomaltooligosaccharides) for PPAR-γ activation and DPP-IV inhibition which shows antidiabetic activity and the FOS was produced from Aspergillus oryzae and IMO’S and standards for 1-kestose,1-nystose,1-frutofuranosyl nystose and panose were procured (32).

Vikas Kumar et al., have reported which shows hypoglycemic effect of wedeloketone isolated from Wedelia calendulae by In-Silicomolecular docking against dipeptidyl peptidase-4(DPP4), glucose transporter-1(GLUT1) and peroxisome proliferator activated receptor-γ(PARA-γ) which shows docking score near -6.17, -9.43 and -7.66 respectively and wedelolactone treat type-2 diabetesmellitus (33).

Abdul Sadiq et al., have reported hyperglycemic activity from Eryngium caeruleum M. Bieb by α-glucosidase by molecular docking studies shows explore possible role of all identified bioactive compound in chloroform fraction of Eryngium caeruleum M. Bieb into active sites of homology model of α-glucosidase which shows antidiabetic activity (34).

Chien-Hung Jhong et al., have reported byIn-Silicomolecular dockingstudies of α-glucosidase and α-amylase inhibitors from natural compounds by molecular docking in-silico and correlation analysis indicated that curcumin and actinodaphinine had high activity α-glucosidase as well as curcumin and berberine for α-amylase inhibitors when compared with acarbose which shows antidiabetic activity (35).

Jayasree Ganugapati et al., have reported In-Silico molecular screening studies of banana flower flavonoids as insulin receptor tyrosine kinase activators as cure for diabetes mellitus by Autodock Vina, Autodock 4.0.to phosphorylated tyrosines docked with hesperitin triacetate, naringenin, naringenin pelargonidin and naringenin flavanone are potent activators of IR tyrosine kinase which shows antidiabetic activity (36).

Noor Rahman et al., have reported In-Silico molecular docking studies of isolated alakaldoids for α-glucosidase inhibition compared with standard acarbose and miglitol were docked to α-glucosidase by molecular dockingstudies of α-glucosidase which shows antidiabetic activity (37).

Muhammad Nadeem et al., have reported antidiabetic byIn-Silicomolecular dockingstudies of potential of leaf extracts and an insight into molecular docking by ethnicanol extract of Calotropis procera and which inhibit α-glucosidase and α-amylase synergistically to prevent hyperglycemic activity (38).

Yang Yang et al., have reported antidiabetic activity byIn-Silicomolecular dockingstudies of potential dipeptidyl peptidase (DPP)-IV inhibitor among Moringa oleifera by phychochemical virtual screening and molecular docking analysis was used to stimulated the interaction mode of candidate compounds with DPP-IV receptors which shows antidiabetic activity (39).

Poonam Kalhotra et al., have reported antidiabetic activity by molecular docking of natural product library reveal chrys in as a novel Dipeptidyl peptidase-IV (DPP-IV) inhibitor by in-silico method.
and in-vitro assay revealed that chrysin inhibits DPP-IV enzyme in a concentration dependent manner shows antidiabetic activity (40).

Olusola Abiola ladokun et al., have reported potent antidiabetic activity of methanolic extract of Hunteria umbellata by molecular docking studies and its compound 2.2-Benzylideneb (3-methyl benzofuran) have significant antidiabetic activity against PPAR-γ and molecular binding interaction shows potent antidiabetic activity (41).

Ajmer Singh Grewal et al., have reported In-Silico molecular docking studies of phenolic compounds from Syzygium cumini by multiple targets of type-2 diabetes and act as antidiabetic agent by in-silico docking study includes α-glucoisidase, dipeptidyl peptidase, glycogen synthase kinase, glucagon receptor catechin and myricetin, quercetin was found to inhibit DPP-IV and develop safe and potent natural type-2 antidiabetic activity (42).

Usman Ghani et al., have reported antidiabetic activity by In-Silico molecular docking studies by natural flavonoid α-glucosidase inhibitors from Retama raetam by molecular docking interaction with enzyme active site and Retamasin D, G, H and Erysuben A and B non-competitively inhibited the enzyme whereas retamasin C and F exhibited competitive inhibition which inhibits α-glucosidase enzyme active site shows antidiabetic activity (43).

Arunugam Sudha et al., have reported In-Silico molecular docking studies of 1,2 disubstituted idopyranose from Vitex negundo by its antidiabetic activity of type-II diabetes ,it manly targets proteins active site (dipeptidyl peptidase-IV and glycogen synthase kinase-III) which results in inhibition of enzyme active site, the binding energy of ligand protein interactions also confirmed that its inhibitory activity (44).

Sudipta Ghosh et al., have reported In-Silico molecular docking and inhibition studies of α-amylase activity by Labdane diterpenes from Alpinia nigra seeds two labdane diterpenes (I and II) fora-amylase inhibitor activity by comparing with standard acarbose among I and II, the diterpene shows highest MolDock and re-rank score to show antidiabetic activity (45).

Pawan Kaushik et al., have reported antidiabetic activity by In-Silico molecular docking studies which shows pharmacophore modeling and molecular docking studies on Pinus roxburghii as target for diabetes mellitus and 17 constituents from Pinus roxburghii were docked on different receptors out of which secosiresinol ,pinoresinol and cededinar showed highest affinity for the aldose reductase and targets are protein tyrosine phosphate-1-β(PTP-1B),dipeptidyl peptidase-IV (DPP-IV),aldose reductase (AR) and insulin receptor with help of docking software Molegro virtual docker(MVD) results of docking score which shows antidiabetic activity(46).

Narasimhamurthy Konappa et al., have reported antidiabetic activity by In-Silico molecular docking studies of Amomum nilgiricum by molecular docking interactions of bioactive serverogenin acetate with target proteins and docking studies were carried out for Phyto ligands using iGEMDock program to elucidate the binding affinities to target proteins targets are α-amylase and α-glucosidase and ligand is serverogenin acetate shows antidiabetic activity (47).

Nausheen Nazir et al., have reported antidiabetic activity byIn-Silico molecular docking studies of Elaeagnus umbellata in Streptozotocin (STZ) induced diabetic rat. Chloroform, ethylacetate extract of potent controlling hyperglycemia in STZ induced type-II diabetes in rats. Molecular docking approach indicated the favorable inhibitory interaction between docked compounds and active site of α-glucosidase and α-amylase andocked compounds occupy binding site as occupied standard acarbose (48).

Da Hye Kim et al., have reported In-Silico molecular docking studies by potential of icarrin metabolites from Epimedium koreanum Nakai as antidiabetic activity, icarin, its deglycosylated icaritin and glycosylated flavonoids (icaeriside II, epimedin A, epimedinB, epimedin C) were evaluated their ability to inhibit protein tyrosine phosphatase 1B(PTP1B) and α-glucosidase. Furthermore, enzyme kinetics analysis and molecular docking shows antidiabetic activity (49).

Chunsheng Zhy et al., have reported antidiabetic activity In-Silico molecular docking studies towards α-glucosidase inhibitor from Clerodendranthus spicatus based on HSCCC coupled by molecular docking method. Among five compounds like 2-caffeoyl-L-tartaric acid, N(E)-Caffeoyl dopamine, rosmarinacidd, methyl rosmarinate,6,7,8,3',4'-pentamethoxy flavone and molecular docking indicated that the affinity energy of identified compounds among them rosmarinic caid which shows antidiabetic activity (50).

Dhiraj Kumar Choudhary et al., have reported In-Silico molecular docking interaction of methanol, acetone extract which gives porcine from Vicia faba crude seed extract and evaluate antidiabetic activity with α-amylase by hydrogen bonding and hydrophobic interaction which shows antidiabetic activity (51).

Rina Herowati et al., have reported antidiabetic activity by molecular docking studies of chemical composition of Tinospora cordifolia on glycogen phosphorylase results indicated that Autodock-vina’s algorithms were valid and the docking result revealed that magnoflorin, cardifoliside A and syrimgin exhibited good binding interaction with active site glycogen phosphorylase shows better anti-diabetic activity (52).

Yan Wang et al., have reported molecular docking screening for identifying hyperoside as an inhibitor of fatty acid binding protein 4 from a natural product and the report as flavanols to be ideal scaffold for FABP4 inhibitor development among popular flavanol (53).

Sudhanshu Kumar bharti et al., have reported antihyperglycemic activity by in-silico molecular docking studies with DPP-IV inhibition of alkaloids from seed extract of Castanospernum austrat by molecular docking studies and berberine which shows competitive inhibition towards DPP-IV by molecular docking studies to normalizes hyperglycemia in type-II
diabetes mellitus rats with strong DPP-IV inhibitory potential activity (54).

Samuel Odeyemi et al., have reported antidiabetic activity by in-silico molecular docking studies by affecting glucose uptake in HepG2 cells following the exposure to methanolic extract of Lauridia tetragna and the α-glucosidase, α-amylase, dipeptidyl peptidase-IV (DPP-IV), lipase inhibitory activities and glucose uptake in HepG2 were investigated which shows good hypoglycemic activity that may be linked to inhibition of crucial enzyme associated with diabetes (55).

Tae Kyung Hyun et al., have reported antidiabetic activity by molecular docking studies for discovery of plant derived α-glucosidase inhibitors which mainly treat type-II diabetes mellitus and α-glucosidase docked with rectine, quercetin and myricetin these can be good patent of α-glucosidase inhibitors act as antidiabetic activity (56).

Channabasava et al., have reported antidiabetic activity by using in-silico molecular docking studies of methanolic extracts of Loranthis microanthus by GEM Dock method and common phytochemical in all extract is octadecenoic acid used separated and used as antidiabetic activity (57).

Pukar Khanal et al., have reported antidiabetic activity by using In-Silico molecular docking studies of Tinospora cordifolia interaction between the compounds, proteins and pathway was interpreted based on edge count. The docking study was performed using Autodock 4.0 and the binding affinity and inhibitory constant of tembatarine with β-1-adrenergic receptor was found to be 6.25 kcal/mol which shows antidiabetic activity (58).

Kiran Kumar Angadi et al., have reported In-Silico molecular docking studies of guggulsterol from Nymphaea pubescens with target glucokinase related to type-II diabetes mellitus which shows good bond interactions by In-Silico method as antidiabetic activity (59).

Muhammad Raza Shah et al., have reported antidiabetic activity by using In-Silico molecular docking studies in which shown by protein tyrosine phosphatase 1B inhibitors isolated from Artemisia roxburghiana and antidiabetic activity of Artemisia roxburghiana could be activated due to PTP1B inhibition by its triterpene constituents like botulin, betulinic acid and taraxeryl acetate against tyrosine phosphatase 1B protein receptor which shows antidiabetic activity (60).

Nur Athirah Zabidi et al., have reported antidiabetic activity by using In-Silico molecular docking of inhibitory evaluation of Curculigo latifolia on α-glucosidase and results phlorin binds strongly with enzyme receptor achieving the lowest binding energy value effective in lowering hyperglycemia (61).

Sathianpong Phoopa et al., have reported antidiabetic activity by using In-Silico molecular docking by chemical constituents of Litsea elliptica and their α-glucosidase inhibition with in-silico method by molecular docking studies and quercetin diglycoside isolated and docked with α-glucosidase enzyme receptor shows antidiabetic activity (62).

Discussion

Diabetes Mellitus is widely spreading diseases due to several lifestyle problems in the 21st century. Treatment and prevention of diabetes is very much essential. Plants are natural reservoir of many medicinal value added components helps to overcome many chronic disorders. Hence herbal medicines are considered to be an excellent remedy for treatment of diabetes mellitus. Molecular docking is an important computational tool to predict the possible interactions between the drug and protein in a non-covalent fashion. Extensive in silico docking procedures have been carried out to examine whether the compound is a good ligand with diabetic targets. Screening of antidiabetic therapeutics is very important and essential for effective management of DM. Many researchers have worked on extraction, isolation, characterization of extracts and bioactive fractions from medicinal plant also they have established profile and data of interaction of active components against various targets and enzymes of DM using In-silico molecular docking tools.

The reviewed articles have extensively concentrated on use of different tools and methods of molecular docking technique. They have extracted, isolated and screened various plant constituents against various targets of DM. Screening included the utilization of different plants from various families and they have isolated constituents which are belongs to the different chemical classes like, alkaloids, glycosides, flavonoids, tannins and diterpene class. Hence the reviewed methods are valuable in identification of important therapeutics from medicinal plants for effective management of DM.

Conclusion

The present review concludes that the management of diabetes mellitus is very important and essential and medicinal plants are natural reservoir of many therapeutic value added components helps to overcome many chronic disorders including diabetes mellitus. In-Silico molecular docking studies and related computational tools are very important and essential in the screening of Anti-Diabetic therapeutics from medicinal plants. Extensive In-Silico docking procedures have been carried out to examine whether the compound is a good ligand with diabetic targets which helps to identify new and important therapeutics for management of diabetes mellitus.

Conflict of Interest

Nil

Abbreviations

1. STZ -Streptozotocin
2. PPAR-γ -Potential peroxisome proliferators activated receptor gamma
3. PTP1B -tyrosine phosphatase 1B
4. DPP-IV-dipeptidyl peptidase-IV
5. MVD-Molegro virtual docker
6. PPL-porcine pancreatic lipase
7. RLR-rat lense aldose reductase
8. HRAR-human recombinant aldose reductase
9. PTP1B- protein tyrosine phosphatase
10. PPL- porcine pancreatic lipase
11. DM: Diabetes Mellitus

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