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In-Silico Analysis of *Abrus precatorius* L. as a Potential Agonist of PPARγ: A Novel Approach to the Treatment of Diabetes

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Abstract

Diabetes mellitus is a chronic disorder that is characterized by a lack of insulin secretion by the pancreas or a defect in insulin action, or both. If diabetes is not controlled, over time it can cause damage to blood vessels and nerves, leading to life-threatening complications such as kidney damage, heart disease, and vision impairment. It can also weaken the immune system, making patients more prone to infection. Although treatments for diabetes have improved over the past few decades, mortality rates due to diabetes and its complications have been on the rise. Moreover, some hyperglycemic agents have been shown to induce irreversible side effects. Therefore, there is an urgent need to explore alternative therapeutic treatments to combat this disease. Peroxisome proliferator-activated receptor gamma (PPARγ) is an important protein that helps regulate glucose levels in the blood. This study explores the potential modulation of PPARγ by phytochemical compounds. In many countries including India, medicinal plants have been used as anti-diabetic agents. Abrus precatorius Linn is an important herb commonly known as rosary pea and abundantly found throughout India. A. precatorius can be used to treat a variety of diseases as various parts of the plants have different pharmacological activity such as anti-diabetic, anti-oxidative, anti-inflammatory, anti-microbial, and neuro-protective effects. The phytochemicals were extracted from the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT). PyRx, an in-silico tool was then used to perform molecular docking simulations to find the lead compounds. The phytochemical compounds kaempferol, carvacrol, abrine, thymol methyl ether, and thymol which had the highest binding affinities with PPARγ were selected for further in-silico analysis and pharmacological evaluation was carried out based on ADMET properties, which was performed in ADMET lab. The compound kaempferol showed the highest binding affinity with PPARγ. Its molecular interaction with PPARγ was captured on Biovia Discovery Studio Visualizer.

Keywords: Diabetes mellitus, *Abrus precatorius* L., peroxisome proliferator-activated receptor gamma (PPARγ), bioinformatics, molecular docking, PyRx, IMPPAT database, Biovia, kaempferol

INTRODUCTION

Insulin is an essential hormone secreted by the β cells of the pancreas. It is crucial for regulating glucose, lipid and carbohydrate metabolism [1]. Glucose is the primary energy source required for our bodies to function efficiently [2]. The pancreatic hormones tightly monitor and regulate blood sugar levels through a process called glucose homeostasis, which is characterized by the balance between glucose production by the liver and glucose utilization by major tissues in the body like liver, adipose, brain, kidney, and muscles. Therefore, in healthy people, an increase in plasma glucose levels results in the increase in secretion of insulin by pancreatic β cells. In addition to glucose homeostasis, insulin is also required for the uptake of glucose in tissues, amino acid transport, DNA

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and protein synthesis, gene transcription and glycogen synthesis. Type 2 diabetes develops when body tissues become resistant to insulin action or when the secretion of pancreatic hormones by the β cells is weakened [3]. According to the latest reports from the International Diabetes Federation (IDF), 1 in 9 adults between the ages of 29 to 79 years is currently battling diabetes. By 2050, current trends show that approximately 853 million adults will be living with diabetes, increasing by 46% [4]. Moreover, it is estimated that 4 in 10 adults are unaware that they have the condition. While there is still no cure for this disorder, treatment options have significantly improved over the past few decades. Currently, treatment of diabetes (type 1 and type 2) includes the use of non-insulin agents (biguanides, sulfonylureas, thiazolidinedione) and insulin (human insulin) [5]. Synthetic treatments have been proven effective, but is generally associated with higher costs, as well as adverse side effects such as coma, liver, and renal disorders [6]. Therefore, there is an increasingly growing interest in whether medicinal plants can limit detrimental side effects associated with current synthetic treatments. Over the past few decades, these therapeutic plants have rapidly spread across the world, with at least 80% of the population relying on some form of herbal medication to treat underlying health conditions [7]. Most importantly, herbal medication is reflective of the indigenous belief systems of local communities in various parts of the world, which has been practiced for centuries. For example, Ayurveda has been the traditional holistic system for the treatment of various diseases in India. Ayurveda and other traditional medicinal systems describe the use of plants to treat diabetes and other conditions. These natural products are not only effective but are also relatively low in cost making it more accessible to the public, especially in poorer countries [8].

Abrus precatorius L. (commonly called Indian licorice) is a woody twinning plant belonging to the family Fabaceae. It is native to India, found at altitudes of up to 1200 meters on the Himalayan borders [9]. Its unique characteristic is its toxic red seeds. Although toxic, its seeds contain several essential amino acids such as valine, alanine, choline, serine, and methyl ester. Through continuous experimentation, researchers have found ways to lower its toxicity, making it a suitable therapeutic product [10]. *A. precatorius* is a rich source of essential phytochemicals, making it an important medicinal plant with valuable therapeutic properties such as neuroprotective, neuromuscular effect, antioxidant, anti-microbial, anti-cancer, anti-viral, and anti-diabetic effects, etc. In relation to diabetes mellitus, a previous study was conducted by introducing 50 mg/kg of the chloroform-methanol extract of *Abrus Precatorius* seeds to diabetic rats induced by the chemical alloxan. The study showed a reduction in blood glucose levels in diabetic rats after treatment with the chloroform-methanol extract at regular intervals, showing that the extract had anti-diabetic effects [11].

Cardiovascular failure is one of the leading causes of the high mortality rates associated with diabetes. Additionally, Type 2 diabetes increases problems in lipid metabolism, hypertension and obesity. Peroxisome proliferator-activated receptor gamma (PPARγ) are ligand-induced transcription factors belonging to the nuclear hormone receptor family. PPARs play a role in controlling the expression of genes involved in lipid, energy, glucose metabolism, inflammation and adipogenesis [12, 13]. PPARγ is a crucial receptor for insulin resistance, even influencing the cardiovascular system. It is an important therapeutic target for inflammation, diabetes, and blood pressure [14]. Currently, thiazolidinedione agents are used as complete agonists of the PPARγ receptor. Although effective in regulating glucose levels, these agents can cause serious side effects, making the search for novel PPARγ agonists critical in battling diabetes [15]. Moreover, research shows that developing partial agonists of the PPARγ can improve side effects, as well as improve cardiovascular problems, inflammation and cancer [14]. Research shows that medicinal plants have the potential to be promising PPARγ agonists. Currently, most identified natural compounds are partial agonists, which bind differently to the receptor, as compared to the full agonist thiazolidinedione. Some natural compounds have shown improvement in diabetic animal models, decreasing side effects, as opposed to synthetic ligand thiazolidinedione [15].

Since the beginning of the 21st century, advancements in science and technology have paved the way for computer-aided drug discovery and design. Drug discovery can be a time-consuming and costly

process. However, bioinformatics tools and techniques have allowed for a more time-efficient and cost-effective drug development, while also improving efficacy of drug candidates [16]. Bioinformatics has been used to screen large-scale biological data, to identify potential binding sites on a protein of interest. Through this integration of computational tools and biological data, bioinformatics has advanced drug target identification, drug characterization and optimization, and prediction of drug-target relationships. Additionally, bioinformatics platforms have been used to characterize side effects, predict drug reactions and resistance, contributing to information on the safety and effectiveness of potential therapeutic targets especially in personalized medication [17, 18]. One such in-silico method that is widely used in drug discovery research is molecular docking.

Molecular docking is an established structure-based molecular modeling technique that is used to predict drug-target interactions to identify therapeutic compounds [19]. Docking involves the orientation or positioning of 3 dimensional structures of a micromolecule (called ligand) to a target binding site on a protein receptor. A variety of docking algorithms and platforms have been developed to predict the active site on proteins, as well as to visualize and study the stable complex formed by the ligand and protein [20]. Molecular docking is mainly performed to predict the activity of a potential drug candidate with a target receptor, and to predict its complementarity through a scoring function. Many drugs fail pre-clinical and clinical trials due to the surfacing of adverse side effects. Molecular docking only requires structural information of the molecules to predict the binding outcome, enabling the early elimination of unfavorable drug candidates. Therefore, molecular docking assists in saving time and cost, making it a valuable part of the drug discovery and development process [19]. In the present study, the ten most valuable phytochemical compounds of *Abrus precatorius L.* were selected. Molecular docking simulations were utilized to evaluate the binding affinity of the compounds with PPARγ. The compounds with the highest binding affinities were then examined for drug-likeness properties and toxicity levels.

PROCEDURE

Retrieval of Ligands

The relevant ligands of the selected medicinal plant were retrieved from the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT) database [https://cb.imsc.res.in/imppat] [21]. The canonical smiles of all the chosen ligands were saved. The top 10 most favorable ligands were chosen, with their structures downloaded from Pubchem [https://pubchem.ncbi.nlm.nih.gov] in SDF format for subsequent analysis [22].

Retrieval of Protein

The Crystal structure of human PPARγ with PDB ID 6VZL was downloaded from the PDB database [https://www.rcsb.org/structure/6VZL]. The protein was downloaded in .PDB format. The protein was obtained at a resolution of 2.07 Å and the method of its retrieval was through X-ray diffraction [23].

Protein Purification

Prior to docking, the obtained protein target PPARγ was first purified. The following procedure was followed – the first step was to remove any water molecules since the crystallographic structure did not match the free energy of the water molecules. All water molecules must be completely removed because they can impact docking scores. To promote more efficient binding with the ligands selected for the study, any ligands that were already bound to the protein were removed. The protein structure was further purified by leaving the A chain intact, while removing the remaining chains. Polar hydrogen atoms were added to improve the purified structure. The entire protein purification process was completed through DS Biovia Discovery Studio [24].

Pharmacological Studies

To analyze the ligands' pharmacological characteristics, SwissADME [http://www.swissadme.ch] analysis was used. The ligands were screened on the criteria of water solubility, GI absorption, bioavailability score, and PAINS and Brenk alerts, following which the best ligands were evaluated

according to the Lipinski rule of five [25]. ADMETLAB 2.0 [https://admetmesh.scbdd.com] was employed to assess the toxicity of the ligands [26]. The utilization of in-silico tools to evaluate pharmacokinetic properties can help prevent failure of potential drug candidates in pre-clinical or clinical trials [27].

Molecular Docking

The purified protein (PPARγ) was uploaded into PyRx virtual screening tools as a macromolecule and the 10 chosen phytochemical compounds were uploaded as ligands. The ligands were converted from .SDF form to .PDB format prior to docking using the OPENBABEL. The grid dimensions of Center X = 13.1707, Center Y= 55.6698 and Center Z = 17.0642 were chosen for the active site. The ligands were docked against PPARγ using the PyRx server and energy minimization was done. The top 5 most effective compounds – Kaempferol, Carvacrol, Abrine, Thymol methyl ether, Thymol were selected for further research based on their binding affinity with the protein target molecule after the docking results were obtained.

Visualization

The structures of the ligands with the top 5 highest binding affinity values were downloaded in .PDB format. The 2D and 3D models of the ligands were produced using Dassault Systems (DS) Biovia Discovery Studio Visualizer [24].

RESULTS

Protein Structure Analysis

A Ramachandran plot is a visual representation of the polypeptide chain angle pairs (ϕ and ψ) of a known protein structure. It is an important tool for studying protein structures [28]. The bioinformatics tool PROCHECK was used to generate the Ramachandran plot for the protein PPARγ, and the secondary structure of the protein was analyzed through PROSITE. The red regions on the Ramachandran plot indicate conformations that are most favorable due to minimal steric clashes. Out of 253 amino acid residues, 211 (92.5%) residues fall in the most favored regions [A,B,L], 16 (7.0%) residues in the additional allowed regions [a, b, l, p], 0 residues in the generously allowed region [-a, -b, -l, -p], and a total of 1(0.4%) residue found in the disallowed region [XX]. Out of the 253 amino acid residues, 228 were identified as non-glycine and non-proline residues, with 11 glycine residues, 9 proline residues and 5 end-residues (Figure 1).

The secondary structure of the protein PPARγ was generated. According to the data received on PDBsum, the secondary structure is shown to have 1 sheet, 2 β hairpins, 4 strands, 4 helices, 26 helix–helix interarchs, 15 β turns and 1 gamma turn (Figure 2).

Pharmacological Evaluation

A compound must meet certain requirements to be employed in drug products. Any potential drug candidate must possess strong absorption, distribution, metabolism, and toxicity (ADMET) properties and must follow the Lipinski rule of 5. This rule is a set of guidelines that predicts the likelihood of the oral availability of the drug based on its adsorption, distribution, metabolism, excretion and toxicity. To ensure the production of medication with as few side effects as possible, a thorough analysis of the compound's toxicity profile is crucial.

The phytocompounds extracted from *Abrus precatorius* were subjected to a pharmacological evaluation to determine their potential therapeutic effects pharmacological evaluation to determine their potential therapeutic effects.

SwissADME Analysis for Drug Likeliness

The physicochemical assessment of the ligands was performed using SwissADME, based on the following criteria (Table 1) – Solubility: Very soluble or soluble, GI absorption: High, bioavailability score: ≥ 0.55, PAINS: 0 alert and Brenk: 0 alert. The physicochemical properties of the top 5 ligands are listed in Table 2.

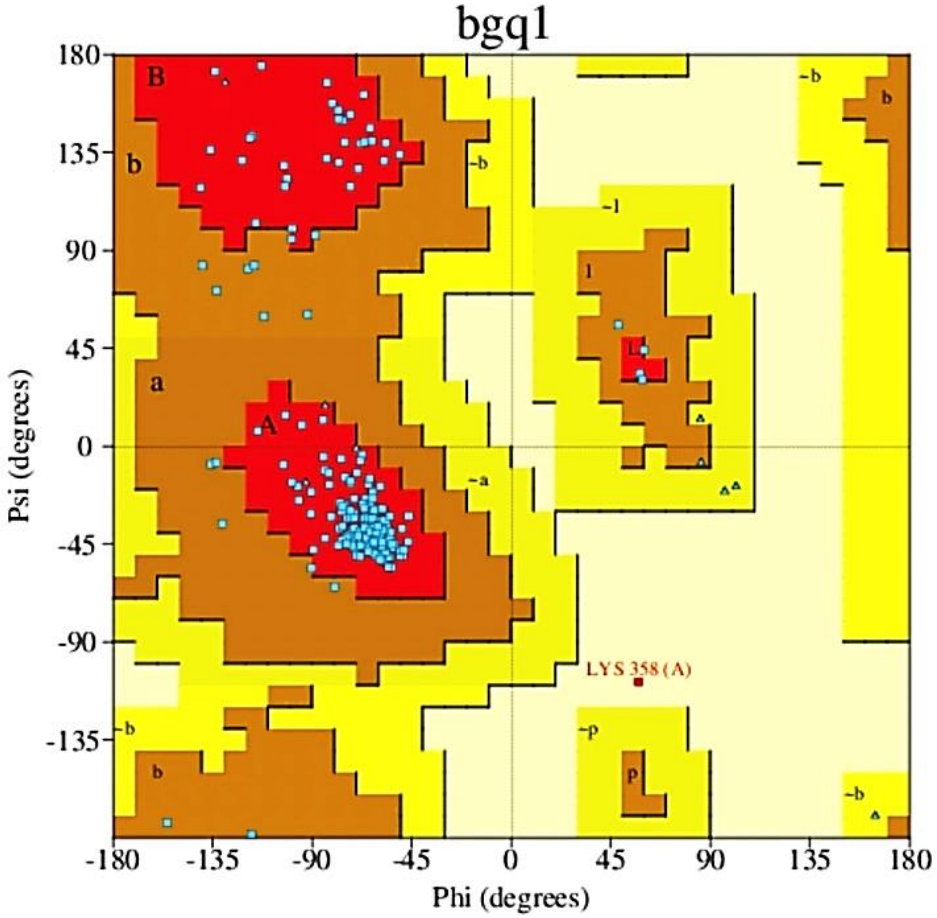

Figure 1. Ramachandran plot of PPARγ protein using PDBsum.

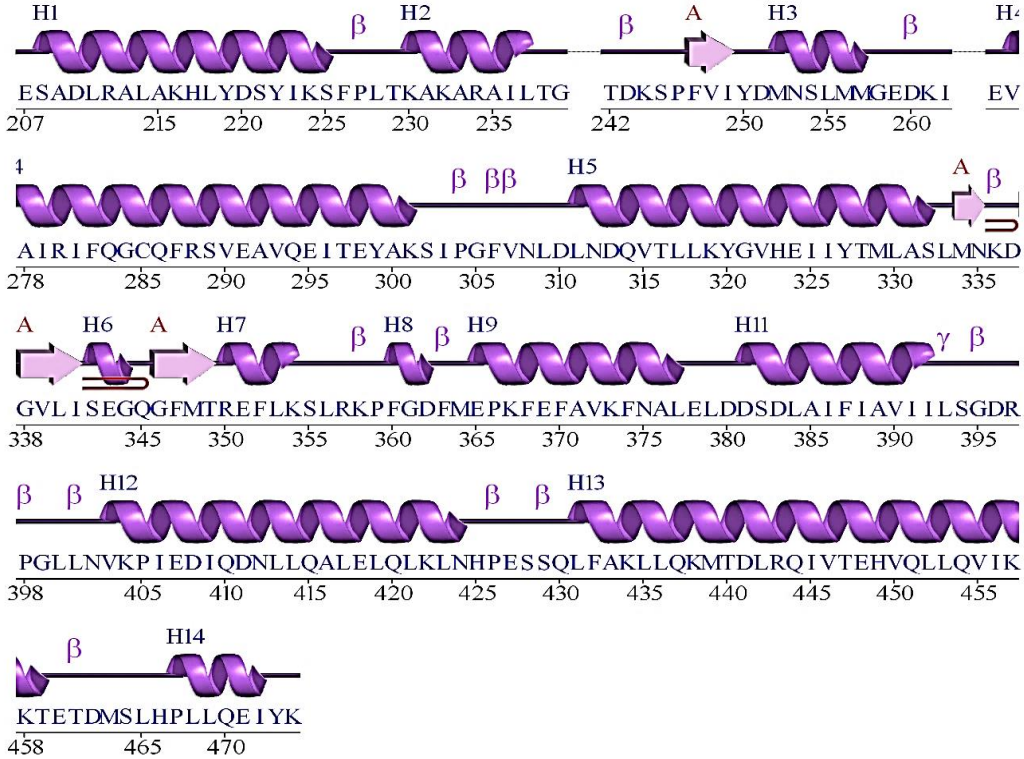

Figure 2. Secondary structure of PPARγ protein using PDBsum.

Table 1. Criteria for physicochemical properties.

Properties	Optimal Range
Solubility	Very soluble, soluble.
GI absorption	High.
Bioavailability score	0.55 and above.
PAINS	0 alerts.
Brenk	0 alerts.

Table 2. Data for physiochemical characteristics of top 5 ligands.

Ligand	Solubility	GI Absorption	Bioavailability Score	PAINS	Brenk
Kaempferol	soluble	High	0.55	0 alerts	0 alerts
Carvacrol	soluble	High	0.55	0 alerts	0 alerts
Abrine	soluble	High	0.55	0 alerts	0 alerts
Thymol methyl ether	soluble	High	0.55	0 alerts	0 alerts
Thymol	soluble	High	0.55	0 alerts	0 alerts

Lipinski's Rule Assessment

The Lipinski rule is a set of five parameters, which are listed in Table 3. It evaluates the drug-likeness and the therapeutic potential of a compound for administration to humans. This rule evaluates drug-likeness based on these criteria: Molecular weight must be 150–500 Daltons, hydrogen bond donors must be <5, hydrogen bond acceptors must be <10, lipophilicity must be <5, octanol-water partition coefficient (LogP) must be <5 and the molar refractivity must be within 40 and 130 Å (Table 3).

As per the results presented in Table 4, the top 5 ligands satisfy the Lipinski rule of 5 without any violations.

Table 3. Lipinski rule criteria.

Properties	Optimal Range
Molecular weight	150–500 Daltons
M logP	<5
H donors	<5
H acceptors	<10
MR	40–130 Å

Table 4. Lipinski rule parameters of top 5 ligands.

Ligand	MW	M LogP	H Donors	H Acceptors	Molar Refractivity
Kaempferol	286.24	–0.03	4	6	76.01
Carvacrol	150.22	2.76	1	1	48.01
Abrine	218.25	–1.38	3	3	62.26
Thymol methyl ether	164.24	3.05	0	1	52.48
Thymol	150.22	2.76	1	1	48.01

ADME Analysis

The ADME analysis has four main characteristics: blood–brain barrier (BBB), glycoprotein transportability (PGP substrate), GI absorption and solubility. This information is crucial for creating medicine. Integrating BBB assessments into ADME analysis helps ensure the effectiveness of a drug and promotes efficient drug formulation. High gastrointestinal (GI) absorption and glycoprotein transportability (PGP substrate) are other key characteristics to consider. The compound should also exhibit good solubility. The data displayed below in Table 5 reveals the fulfilment of the required criteria by all the ligands.

Table 5. ADME analysis data retrieved from SwissADME.

Ligand	BBB	GI Absorption	PGP Substrate	Solubility (LOGSw-SILICOS IT)
Carvacrol	yes	High	no	–3.01
Abrine	yes	High	no	–3.56
Thymol methyl ether	yes	high	no	–3.73
Thymol	yes	high	no	–3.01
Kaempferol	no	high	no	–3.82

Toxicity Prediction

Some of the key characteristics of toxicity prediction are skin sensitivity, carcinogenicity, respiratory toxicity, AMES toxicity, Rat Oral Acute Toxicity, FDAMDD, hERG blockers, H-HT, and DILI. These parameters were evaluated to determine the toxicity of the top 5 ligands (Table 6).

Table 6. Toxicity profile of ligands obtained from ADMET lab and ProTox server.

Ligand	hERG	H-HT	DILI	Ames	ROA	Carcinogenicity	Respiratory	Skin Sensitivity
Carvacrol	0.012	0.031	0.085	0.034	0.217	0.269	0.198	0
Abrine	0.041	0.272	0.087	0.012	0.915	0.184	0.582	0
Thymol methyl ether	0.024	0.052	0.519	0.043	0.063	0.468	0.046	0
Thymol	0.011	0.032	0.137	0.053	0.276	0.287	0.603	0
Kaempferol	0.07	0.098	0.979	0.672	0.156	0.097	0.09	4

Molecular Docking

The binding affinity of the chosen ligands toward the PPARγ protein was obtained by PyRx (Table 7). The ligand with maximum binding affinity was selected for further analysis. The compounds which showed the highest binding energy were Kaempferol, Carvacrol, Abrine, Thymol methyl ether, Thymol. These compounds showed a binding affinity of more than –6.1 (Table 7).

Table 7. Binding affinities of the ligands towards PPARγ protein.

Ligand	Binding Affinity With PPARγ Protein
Kaempferol	–7.5
Carvacrol	–6.3
Abrine	–6.2
Thymol methyl ether	–6.2
Thymol	–6.1

Visualization

The ligand Kaempferol with a binding affinity of –7.5, had the least binding energy with the target protein PPARγ. The receptor-ligand interaction of Kaempferol and PPARγ protein was visualized in BIOVIA Discovery Studio Visualizer. The 2D and 3D structure of the binding interaction was obtained, which is displayed in Figures 3 and 4. From the structures, it is evident that the ligand interacts with amino groups like LYS, TYR, GLU, VAL, ARG.

DISCUSSION

Diabetes mellitus is a chronic disease that is caused by the inherited or acquired ineffective or insufficient secretion of insulin from the pancreas. Diabetes leads to many long-term complications, such as cardiovascular conditions, neuropathy, nephropathy, and ulcerations, which is what makes this disease so devastating [29]. Diabetes can be divided into two major types: Type 1 and Type 2 diabetes. Type 1 diabetes mellitus is an autoimmune disease, that is caused by the destruction of the pancreatic β cells, leading to a lack of insulin secretion. Type 2 diabetes is not an autoimmune disease but is caused by a combination of genetic and environmental factors such as a deficiency in insulin secretion, insulin resistance, obesity, an unhealthy diet, lack of exercise, and a sedentary lifestyle [30].

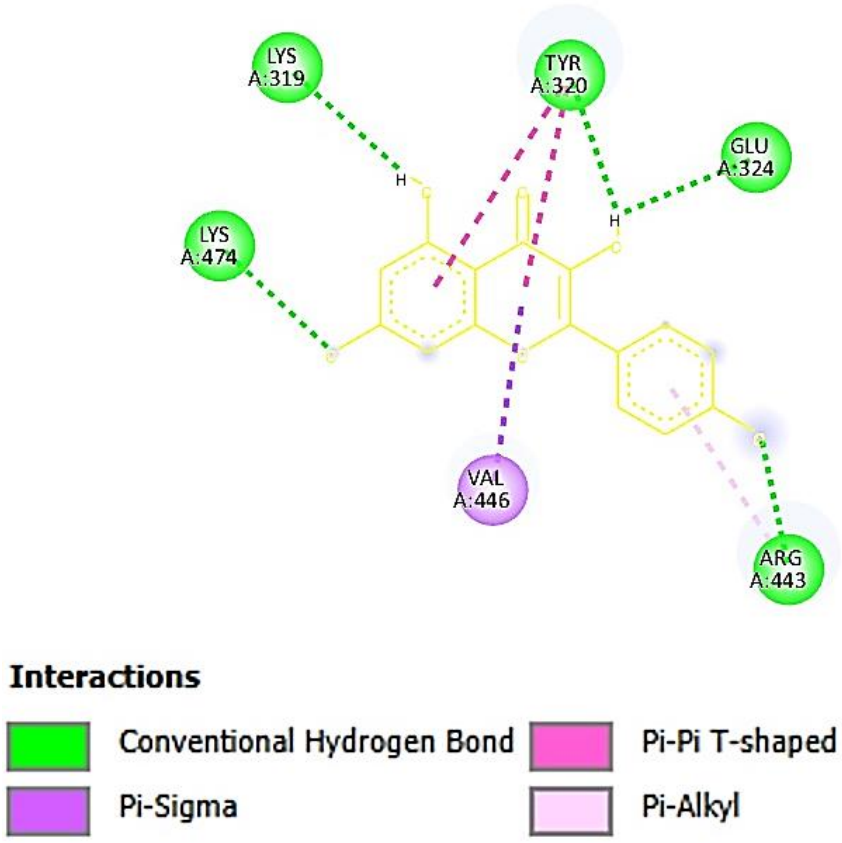

Figure 3. 2D structure of interactions between PPARγ protein and Kaempferol ligand.

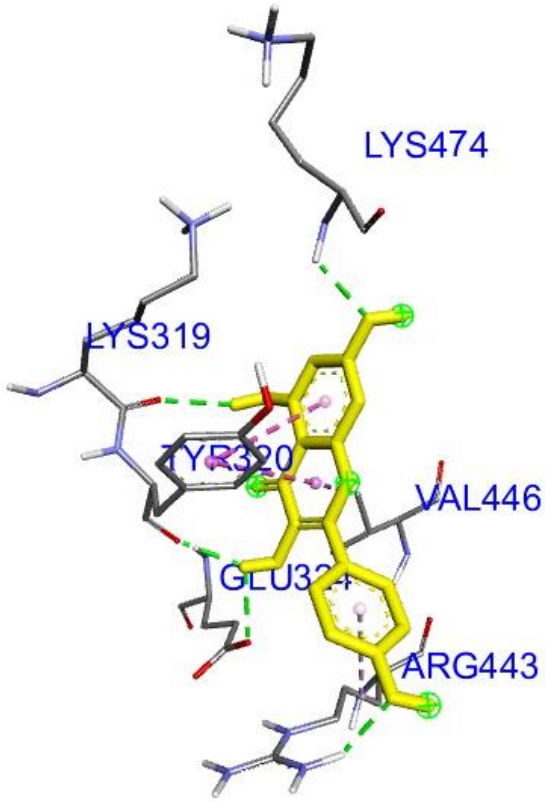

Figure 4. 3D visualization of interactions between PPARγ protein and Kaempferol.

Drugs are used to save lives and to combat the underlying metabolic conditions, such as the decrease in insulin secretion, and insulin resistance, thereby alleviating symptoms. Insulin replacement therapy is used as a treatment for Type 1 diabetic patients. Insulin is also used for Type 2 diabetes when blood glucose levels cannot be managed by exercise, diet, and oral medications. The main oral anti-diabetic drugs include sulphonylureas, alpha glucosidase inhibitors, thiazolidenediones, and biguanides. Although these oral medications are effective in lowering glucose levels in the blood, they come with side effects [29]. Some side effects include digestive discomfort, weight gain, allergic reactions, hypoglycemia, hepatotoxicity, edema, and heart failure [31–33]. Pharmaceutical companies spend millions of dollars per drug, only for majority of the drugs to fail in reaching the market. One of the main challenges the pharmaceutical industry faces in the drug development process is the development of adverse drug reactions. The increasing need to produce more effective drugs with low risk, in a short period of time has sparked interest in bioinformatics. Bioinformatics provides databases and software for identifying and validating drug targets, which helps to minimize failure in clinical trials. Adverse side effects from drugs are one of the main causes of deaths worldwide, which also causes a loss of confidence in the healthcare system. Bioinformatics provides new opportunities to combat this problem. One such strategy is through personalized medication, which allows to produce drugs based on an individual's genetic makeup, thereby significantly reducing unfavorable drug effects [34].

For centuries, traditional healthcare systems have utilized the benefits of medicinal plants to treat several diseases, including diabetes. However, medicinal plants typically have hundreds of compounds, making it difficult to study the biological and pharmacological benefits of the plant. Over the past few decades, bioinformatics has contributed to a shift in research from a single, isolated mode to a more holistic approach in traditional medicine, where the molecular mechanisms of herbal plants can be studied [35]. In this study, phytochemicals extracted from *Abrus precatorius L.* as potential agonists of the PPARγ, were evaluated.

Peroxisome proliferator-activated receptor gamma (PPARγ) is a target for insulin sensitization which controls the expression of hexokinase and inhibits G6Pase, thereby modulating glucose homeostasis and the action of insulin. It is a molecular target for various medications that treat multiple metabolic disorders [20]. Furthermore, PPARγ activation is linked to better cardiovascular health.

In conventional drug discovery programs, molecular docking is a useful tool for predicting interactions of all molecules with drug target(s) to guide medicinal decisions. Efforts have been made to include molecular docking techniques into natural products-based drug discovery [17]. The results of the current study demonstrated that the five phytocompounds Kaempferol, Carvacrol, Abrine, Thymol methyl ether, Thymol showed the highest binding affinity of more than –6.1. Kaempferol specifically showed the highest binding affinity of –7.5. Kaempferol (3,5,7-trihydroxy-2-[4-hydroxyphenyl]-4H-1-benzopyran-4-one) is a natural flavonoid. Flavonoids are plant-derived products and are the largest group of secondary plant metabolites. They are used by the plant to regulate its growth and for defense [36]. Kaempferol can be found in many fruits and vegetables, some of which are onions, strawberries, beans, cabbage, chia seeds, garlic, broccoli and grapes [37, 38]. Kaempferol has anti-cancer [38], anti-inflammatory [39], anti-alzheimer [40], anti-diabetic [41], anti-microbial [36], and cardiovascular effects [41]. The accumulation of free fatty acids leads to cell dysfunction, causing β cells apoptosis and insulin resistance, which leads to the progression of diabetes. Kaempferol also regulates glucose production and utilization. Insulin resistance causes abnormal levels of glucokinase (GCK), an enzyme responsible for regulating blood glucose levels. Kaempferol promotes the activation of GCK, thereby decreasing blood glucose levels. Kaempferol also shows reduction in oxidative stress and protects pancreatic β cells [42]. In addition, carvacrol has been studied in diabetes animal models. It is known to reduce blood glucose levels by interacting with diabetes related enzymes as well as lowering heart problems [43]. It improves glucose uptake, insulin resistance, inflammation and oxidative stress. Carvacrol in combination with other hyperglycemic agents could be a powerful anti-diabetic treatment [44]. While *Abrus precatorius* is a versatile plant with numerous health benefits, a deeper understanding of its therapeutic potential and the activation of PPARγ and its mechanism is required for the development of novel therapeutic methods for the treatment of diabetes.

CONCLUSIONS

Over the past few decades, computational drug discovery has contributed to novel insights on the pathology of diseases and their cures. Moreover, computational pharmacological evaluation has paved the way for unraveling the complex mechanisms of multi-component therapeutic plants. The current study presents a comprehensive evaluation of the medicinal plant *Abrus precatorius L.* and its interaction with the protein PPARγ. Molecular docking results revealed that kaempferol had the highest binding affinity with PPARγ. This flavanol binds to the target with a binding affinity of –7.5, displaying a partial modulation of the PPARγ receptor. Therefore, the docking result presents *Abrus precatorius L.* as a promising therapeutic source for the treatment of diabetes mellitus. Previous studies confirm that the partial activation of the PPARγ receptor could reduce adverse side effects associated with full agonists. However, additional research is required to explore the medicinal benefits of *Abrus precatorius* in the treatment of diabetes mellitus. In general, drug discovery from natural sources is a complex process, combining botanical, physiochemical, biological and molecular techniques. At present, medicinal-plant-based drug discovery remains an interesting and viable area, where a systematic search can lead to promising leads against various disease targets.

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Conflicts of Interest

The authors declare no conflict of interest.

Funding

Nil.

Abbreviations

A. precatorius L.	*Abrus precatorius Linn*
BBB	Blood–Brain Barrier.
ADMET	Absorption, Distribution, Metabolism, Excretion and Toxicity
DILI	Drug-Induced Liver Injury.
DNA	Deoxyribonucleic acid.
DS	Discovery Studio.
FDAMDD	Food and Drug Administration Minimum Drug Development Data.
GCK	Glucokinase.
hERG	Human ether-à-go-go-related gene.
H-HT	Human Hepatotoxicity.
IDF	International Diabetes Federation.
IMPPAT	Indian Medicinal Plants, Phytochemistry and Therapeutics.
PPARγ	Peroxisome proliferator-activated receptor gamma.

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