(ISSN: 0973-7049(P))

The Bioscan AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES 21(4): 481-502 2026 www.thebioscan.com

# Integrated GC-MS Based Phytochemical Profiling, Network Pharmacology, Molecular Docking and Molecular Dynamics Reveal the Multitarget Anti-Diabetic potential of Ricinus communis Leaf Phytoconstituents

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DOI: https://doi.org/10.63001/tbs.2026.v21.i04.pp481-502

**KEYWORDS**

*Ricinus communis; GC-MS analysis; Network pharmacology; antidiabetic activity; Molecular Docking; PI3K-AKT signalling pathway.*

**Article Info**

**Received:26.10.2026**

**Accepted: 14.11.2026**

**Published: 24.11.2026**

## Abstract

Diabetes mellitus is a chronic metabolic disease that is associated with impaired glucose metabolism, insulin resistance, oxidative stress and causes serious systemic complications. In the present study, the bio-phytochemical profile analysis, pharmacokinetic analysis, network pharmacology, molecular docking and molecular dynamics simulation studies were performed to explore the antidiabetic potential of bioactive phytoconstituents of the leaf extract of Ricinus communis in an integrated approach. Solvent extraction was carried out on leaves of Ricinus communis followed by Gas Chromatography–Mass Spectrometry (GC–MS) analysis for the phytochemical identification. Several biologically active compounds such as β-sitosterol, oleic acid, ricinoleic acid, phytol, squalene, caryophyllene and fatty acids derivatives were identified by the GC–MS profile. SwissADME analysis was used to demonstrate the selected compounds to have favourable drug-likeness and pharmacokinetic properties, among which β-sitosterol, oleic acid, ricinoleic acid and phytol were the compounds that showed most favourable properties. Major proteins that are affected by diabetes like AKT1, PPARG, TNF, IL6, PIK3CA, DPP4, MAPK1 were predicted using Swiss Target Prediction. The genes related to diabetes were obtained from GeneCards, OMIM and DisGeNET database and Venn analysis was conducted to obtain overlapping targets. The hub genes AKT1, PPARG, TNF and PIK3CA were identified, all of which are associated with insulin signalling, inflammatory regulation and glucose metabolism, through protein–protein interaction analysis using STRING and compound–target network construction using Cytoscape. Overall, functional enrichment analysis with Metascape revealed significant enrichment of PI3K–AKT signalling pathway, AGE–RAGE signalling pathway in diabetic complications, leptin signalling, oxidative stress response and inflammatory pathways. Molecular docking revealed high binding affinity of β-sitosterol with PPAR-γ and ricinoleic acid with α-glucosidase indicating its potential to be used in insulin sensitizing and carbohydrate metabolism regulation, respectively. The stability of the protein–ligand complexes was also confirmed by molecular dynamics simulations. Overall, the results obtained suggested a multitarget action of the phytoconstituents found in the leaves of Ricinus communis, highlighting their potential applications in diabetes treatment and drug development research.

## 1.0. Introduction

Diabetes mellitus is a common chronic metabolic condition in the world and is defined as a sustained hyperglycaemia resulting from impaired insulin secretion and/or insulin resistance (Powers et al., 2022). It is estimated that the prevalence of diabetes mellitus remains a constantly increasing problem, mainly caused by lifestyle changes, sedentary behaviour, overweight and obesity, and genetic factors (Arokiasamy et al., 2021). Chronic hyperglycaemia can lead to serious complications such as cardiovascular diseases, nephropathy, neuropathy, retinopathy and oxidative stress-induced tissue damage (González et al., 2023). There are currently several synthetic antidiabetic drugs, but they have numerous side effects, they become less effective over time, they may become resistant, and the treatment is expensive (Blahova et al., 2021). Therefore, the search for natural therapeutic agents that are safe and effective has been of great interest in recent years (Naeem et al., 2022).

Medicinal plants have been used as the sources of bioactive compounds, which have therapeutic potential against various metabolic disorders since ancient times (Ansari et al., 2025). Among these, Ricinus communis L. Castor plant (Ricinus communis L.) is a

member of the Euphorbiaceous family which is widely used and distributed in the tropical and sub-tropical parts of the world and is traditionally used in folk medicine for the treatment of inflammation, infection, gastrointestinal disorders and metabolic diseases (Chouhan et al., 2021). Pharmacological activities like antioxidant, antimicrobial, anti-inflammatory, hepatoprotective and antidiabetic properties have been reported for various parts of the plant-leaves, seeds, roots and oil-of the plant (Cherrada et al., 2024). The therapeutic properties of Ricinus communis are mainly attributed to its rich phytochemical composition that includes fatty acids, Terpenoids, sterols, phenolic compounds and flavonoids (Raza et al., 2026).

Phytoconstituents of plant extracts were volatiles and semi-volatiles and were identified using Gas Chromatography–Mass Spectrometry (GC-MS) technique, which is very useful technique (Mutha et al., 2025). GC–MS analysis is a useful technique which aids in identification of bioactive compound which in turn provides an insight into the chemical composition of medicinal plants and its probable pharmacological action (Ralte et al., 2022). In many cases, however, biological action of phytocompounds is mediated by several molecular targets and signalling pathways, making advanced computational approaches needed for the understanding of the mechanism of action (Chihomvu et al., 2024).

Network pharmacology is a systems biology method which has been proven to be a valuable tool in understanding complex interactions between phytocompounds, target proteins, biological pathways, and diseases (Noor et al., 2022). The network pharmacology approach breaks away from the “one drug–one target–one pathway” paradigm, which characterizes the therapeutic mechanism of single targets and single pathways, and is suitable for studies on multipath and multiprotein interactions in the mechanisms of action of herbal medicines and complex metabolic diseases such as diabetes mellitus (Li et al., 2023). Furthermore, molecular docking and molecular dynamics simulation provide structural and energetic insights into the protein-ligand interaction and help to confirm the stability of protein-ligand binding of phytochemicals in relation to therapeutic targets (Akash et al., 2023).

In this present investigation an integrated approach of computational and phytochemical approach was used to study the antidiabetic potential of Ricinus communis leaf extract (Chakraborty et al., 2026). GC–MS analysis was also carried out to identify the major bioactive compounds followed by SwissADME evaluation, target prediction, network pharmacology analysis, protein–protein interaction studies, functional enrichment analysis, molecular docking and molecular dynamics simulation studies (Das et al., 2022). The purpose of the study was to unravel the molecular mechanism of the antidiabetic activity of Ricinus communis phytoconstituents, and to determine potential molecular targets linked to insulin signalling and glucose metabolism, inflammatory regulation and oxidative stress pathways (Ramothloa et al., 2025).

Diabetes mellitus is one of the most prevalent chronic metabolic diseases in the world, and it is characterised by hyperglycaemia that persists as a result of a decrease in insulin secretion, an increase in insulin resistance or both (Powers et al. 2022). Reports from the global health indicate that the incidence of diabetes mellitus is still escalating rapidly because of the lack of physical activities, obesity, unhealthy eating habits and genetic susceptibility (Arokiasamy et al., 2021). High blood glucose levels over time can lead to serious conditions like cardiovascular disease, kidney disease, nerve damage (neuropathy), eye damage (retinopathy) and damage to tissues from oxidative stress (González et al., 2023). Several

synthetic antidiabetic agents are available, but their long-term use can lead to side effects, decreased effectiveness, drug resistance and high cost of treatment (Blahova et al., 2021). Thus, in recent years, the quest for safer and effective natural therapeutic agents has been attracting a lot of attention (Naeem et al., 2022).

Medicinal plants have been used as a source of bioactive compounds that have therapeutic potential for various metabolic disorders since ancient times (Ansari et al., 2025). Of these, Ricinus communis L. The castor plant (Ricinus communis), a member of the Euphorbiaceous family, is found in tropical and subtropical areas, and has been used in folk medicine for treating inflammation, infections, gastrointestinal disorders and metabolic diseases (Chouhan et al., 2021). The plant's leaves, seeds, roots and oil have been reported as having a range of pharmacologic activities, such as antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, and antidiabetic properties (Cherrada et al., 2024). The therapeutic properties of Ricinus communis are mainly due to the presence of its phytochemical properties which consist of fatty acids, Terpenoids, sterols, phenolic compounds, and flavonoids (Raza et al., 2026).

The Gas Chromatography–Mass Spectrometry (GC–MS) is a very useful analytical technique and has been widely used for identification of the volatile and semi-volatile phytoconstituents present in the plant extracts (Mutha et al., 2025). GC–MS studies can be employed to determine the bioactive compounds which can be used to gain insight of the chemical composition and potential pharmacological activity of medicinal plants (Ralte et al., 2022). The molecular effects of phytocompounds on different targets at the molecular level could have multiple molecular targets and/or pathways, leading to the need for advanced computational tools for the understanding of the mechanisms (Chihomvu et al., 2024).

Network Pharmacology is an effective systems biology tool that can be employed to explain complex interactions between phytocompounds, target proteins, biological pathways and diseases (Noor et al., 2022). The “one drug–one target” approach is different from a network pharmacology approach, which emphasizes multiple targets and multipath effects, providing a high potential for the study of the drugs from the herbal medicine and complex metabolic diseases such as diabetes mellitus (Li et al., 2023). Moreover, molecular docking and molecular dynamics simulations provide structural and energetic insights into protein–ligand interactions and confirms the binding stability of the phytocompound with the therapeutic target proteins (Akash et al., 2023).

The present study was based on the integrated computational and phytochemical approach to explore the anti-diabetic activity of Ricinus communis leaf extract (Chakraborty et al., 2026). The major bioactive compounds were identified by GC–MS analysis followed by SwissADME evaluation, prediction of target, network pharmacology analysis and protein–protein interaction study, functional enrichment analysis, molecular docking, molecular dynamics simulation studies (Das et al., 2022). The aim of the present study was to gain insight into the multi-target molecular mechanisms underlying the antidiabetic properties of phytoconstituents from Ricinus communis and to identify potential therapeutic targets associated with insulin signalling, glucose metabolism, inflammation and oxidoreduction pathways (Ramothloa et al., 2025).

## 2.0. Methodology

### 2.1 Collection and Preparation of Plant Material

Fresh leaves of *Ricinus communis L.* were collected from the local region and authenticated based on morphological

characteristics *(Nour et al., 2023)*. The collected leaves were thoroughly washed with distilled water to remove dust and impurities, shade dried at room temperature for 10–15 days, and pulverized into fine powder using a mechanical grinder *(Mekonnen et al., 2026)*. The powdered material was stored in an airtight container until further analysis *(Bashir et al., 2022)*.

**2.2 Preparation of Plant Extract**

Approximately 25 g of powdered leaf material was subjected to solvent extraction using methanol by Soxhlet extraction method. The extraction process was carried out for 6–8 h until complete extraction of phytoconstituents was achieved *(Olunusi et al., 2025)*. The obtained extract was filtered using Whatman No.1 filter paper and concentrated using a rotary evaporator under reduced pressure. The concentrated extract was stored at 4°C for further phytochemical and computational analyses *(Bhat et al., 2025)*.

**2.3 GC–MS Analysis**

Gas Chromatography–Mass Spectrometry (GC-MS) analysis of the methanolic leaf extract was performed to identify the bioactive phytoconstituents present in Ricinus communis *(Manzoor et al., 2025)*. The analysis was carried out using a GC-MS instrument equipped with a capillary column and helium as carrier gas. The injector temperature was maintained at 250°C with a programmed oven temperature ranging from 60°C to 300°C *(Margolin Eren et al., 2022)*. The ionization energy was maintained at 70 eV. Compounds were identified based on retention time, mass spectral fragmentation pattern, and comparison with NIST library database *(Elkabets et al., 2020)*.

**2.4 Retrieval of Phytocompounds and Canonical SMILES**

Major phytocompounds identified through GC–MS analysis were selected based on peak area percentage and pharmacological relevance *(Singh et al., 2023)*. Canonical SMILES and molecular information of the selected compounds were retrieved from the PubChem Database for further computational analysis (*Nguyen et al., 2024)*.

**2.5 SwissADME Analysis**

Drug-likeness and pharmacokinetic properties of the selected phytocompounds were evaluated using the SwissADME Web Tool *(Riyadi et al 2021)*. Parameters including molecular weight, lipophilicity, polarity, solubility, and gastrointestinal absorption, Lipinski's rule of five, bioavailability radar, and flexibility were analyzed to assess the suitability of compounds for oral drug development *(Pirzada et al., 2024)*.

**2.6 Prediction of Potential Targets**

Potential protein targets of the selected phytocompounds were predicted using the SwissTargetPrediction Server (*Krishnasamy et al., 2025*). Canonical SMILES of each compound were used as input, and the target species was restricted to Homo sapiens (*Vaghela et al., 2026)*. Predicted targets associated with diabetes mellitus and metabolic regulation was selected for further network pharmacology analysis *(Ye et al., 2025)*.

**2.7 Identification of Diabetes Mellitus-Associated Genes**

Diabetes mellitus-related genes were retrieved from public disease databases including GeneCards, DisGeNET, and OMIM using keywords such as "Type 2 Diabetes Mellitus," "hyperglycemia," and "insulin resistance" *(Meng et al., 2026)*. Duplicate genes were removed, and relevant genes were selected based on association scores *(McClelland et al., 2026)*.

**2.8 Venn Analysis of Common Targets**

Common targets between phytocompound-predicted targets and diabetes-associated genes

were identified using the Venny 2.1 Tool. The overlapping genes obtained from Venn analysis were considered potential therapeutic targets involved in the antidiabetic activity of Ricinus communis phytoconstituents *(Chakraborty et al., 2026).*

### 2.9 Protein–Protein Interaction (PPI) Analysis

The overlapping targets were imported into the STRING Database to construct the protein–protein interaction (PPI) network. The organism was set to Homo sapiens, and the confidence score was maintained at >0.7 *(Polaki et al., 2026).* The generated interaction network was exported and visualized using Cytoscape Software to identify hub genes and interaction patterns *(Bathla et al., 2026).*

### 2.10 Compounds-Target Network Construction

Compound–target interaction networks were constructed using Cytoscape software based on the relationships between selected phytocompounds and predicted therapeutic targets *(Rahimi et al., 2026*). Network topology parameters including degree centrality and node interactions were analyzed to identify major hub compounds and proteins associated with antidiabetic activity *(Ononamadu et al., 2024).*

### 2.11 Functional Enrichment Analysis

Functional enrichment analysis including Gene Ontology (GO) and Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathway analysis was performed using Metascape (*Jain et al., 2024)*. Significant biological processes, molecular functions, cellular components, and signaling pathways associated with the overlapping targets were identified. Pathways with p-value < 0.05 were considered statistically significant (*Shah et al., 2025).*

### 2.12 Molecular Docking Analysis

Molecular docking studies were performed to evaluate the binding affinity of selected phytocompounds toward major diabetes-associated target proteins including PPAR-γ, α-glucosidase, and DPP4 (*Tasnim et al., 2024).* Three-dimensional structures of target proteins were retrieved from the Protein Data Bank (PDB) (*Guzenko et al., 2020).* Protein preparation, ligand minimization, and docking studies were carried out using PyRx software integrated with AutoDock Vina (*Naveed et al., 2025*). Binding affinity values and interaction profiles were analyzed using Discovery Studio Visualizer.

### 2.13 Molecular Dynamics Simulation

The stability of selected protein–ligand complexes was evaluated through molecular dynamics simulation using WebGRO. The docked complexes were subjected to 50 ns simulation under physiological conditions (*Javid et al 2024).* Parameters including root mean square deviation (RMSD), root mean square fluctuation (RMSF), hydrogen bond interactions, and radius of gyration were analyzed to assess the stability and dynamic behaviour of the complexes *(Janakiramulu et al., 2025).*

### 2.14 Statistical and Computational Analysis

All computational analyses were performed using standard default parameters provided by the respective software and databases. The generated networks, enrichment analyses, docking scores, and molecular dynamics results were interpreted based on biological relevance to diabetes mellitus and associated signalling pathways *(Pokhrel et al., 2025).*

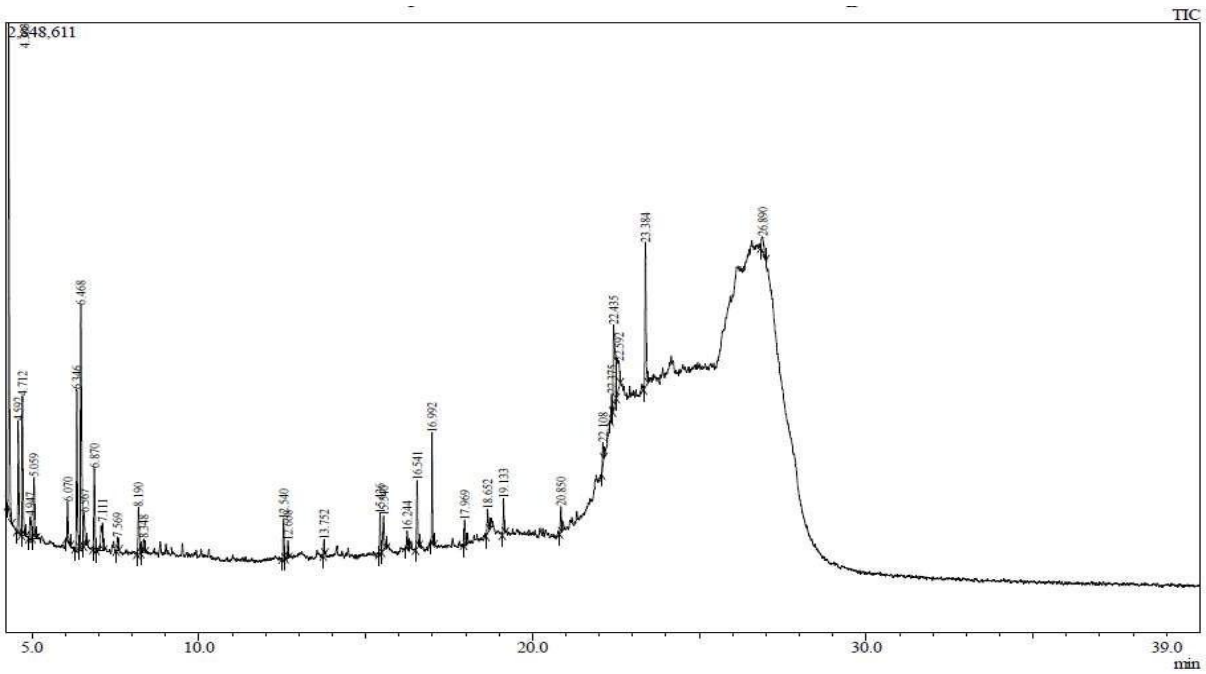
## 3.0. Results

### 3.1 GC-MS Analysis of Ricinus communis Leaf Extract

The methanolic extract of *Ricinus communis* leaves on GC-MS analysis was found to contain some phytoconstituents that have biological activities of varying

pharmacological significance. The chromatogram showed several peaks identified as compounds of fatty acids, Terpenoids, phytosterols, alcohols, aldehydes and lipid derivatives. Major compounds identified were β-sitosterol, oleic acid, ricinoleic acid derivative, phytol, squalene, caryophyllene, palmitic acid and stearic acid. From the identified compounds, the compound with the highest peak intensity was β-sitosterol which showed it to be present in large amounts in the extract. Other significant constituents were oleic acid and ricinoleic acid derivatives, which may be responsible for the antidiabetic and anti-inflammatory properties reported by the plant extract. The identified phytoconstituents are known to have antioxidant, insulin-sensitizing, anti-inflammatory and glucose-regulating properties.

**Figure 1 : GC-MS chromatogram of extract of *Ricinus Communis***




### 3.2 SwissADME Analysis

The pharmacokinetics and drug likeness properties of some bioactive compounds were evaluated using SwissADME analysis. It was found that the majority of the compounds had good physicochemical properties such as good lipophilicity, molecular flexibility, gastrointestinal absorption and mouth to gut bioavailability. Since both oleic acid and ricinoleic acid exhibited good membrane permeability and acceptable bioavailability radar properties, along with a balanced pharmacokinetic profile, β-Sitosterol which is more hydrophobic, has been suggested to have better receptor binding interactions and lower aqueous solubility. In general, the compounds selected exhibited good drug-like properties for further computational studies.

(ISSN: 0973-7049(P))

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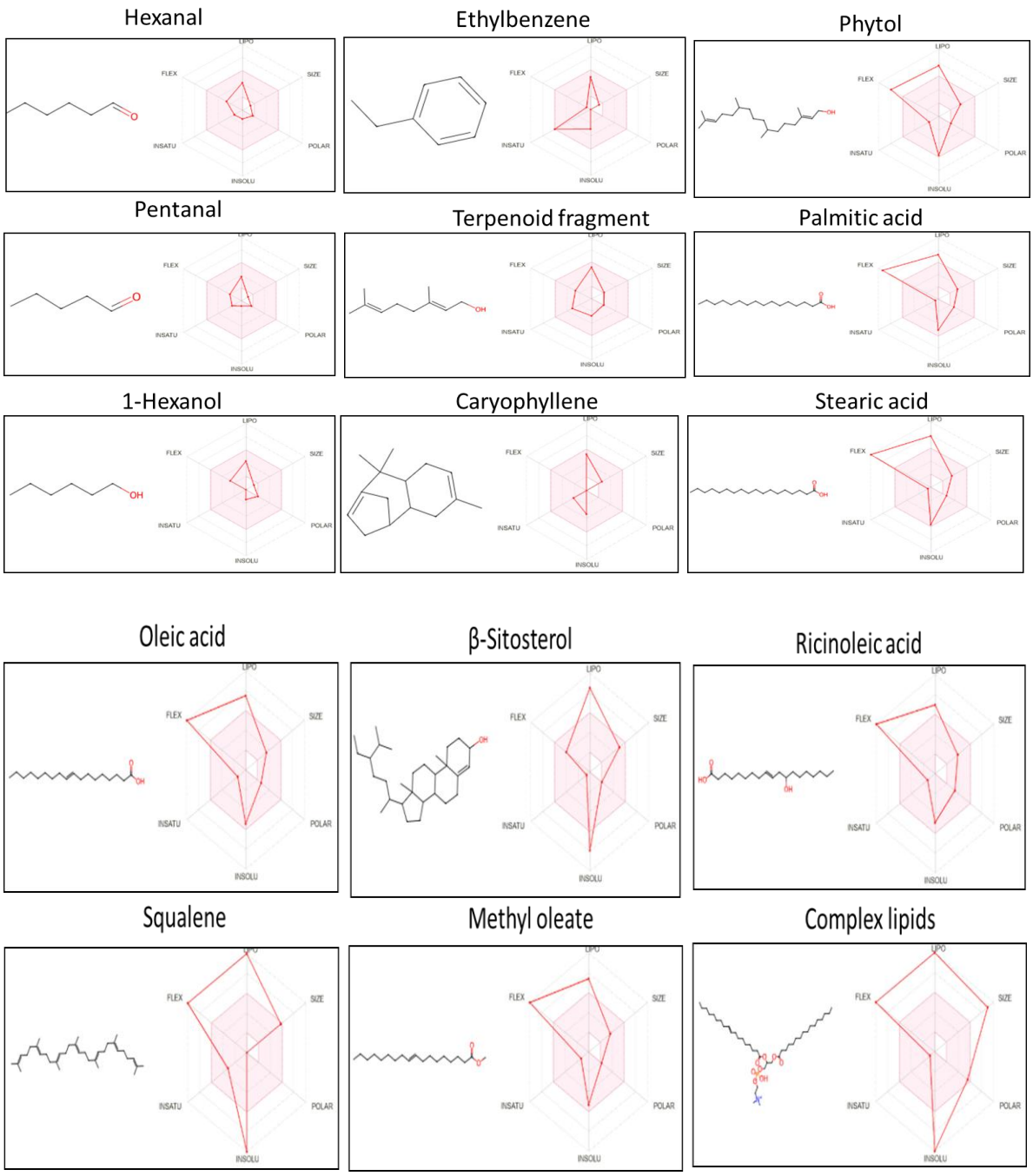
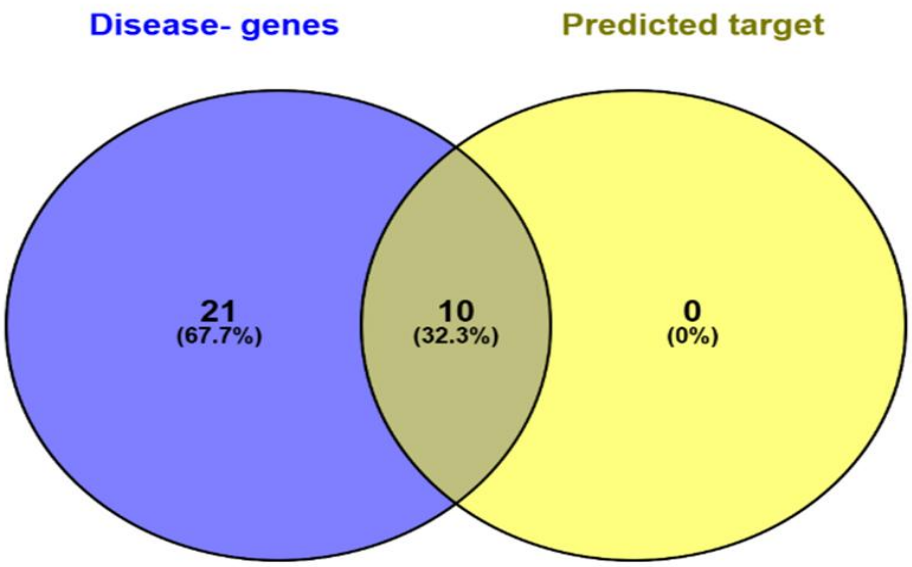
**Figure 2 :SWISS ADME properties of Bioactive principles of *Ricinus Communis***




### 3.3 Prediction of Potential Targets

Swiss Target Prediction analysis predicted that the selected phytocompounds target several diabetes associated molecular targets, which include PPARG and AKT1 for β-Sitosterol and insulin sensitization and glucose metabolism regulation, respectively. Oleic acid had interactions with AKT1 and PIK3CA, indicating potential roles in the insulin signalling pathways involving PI3K-AKT pathway. Ricinoleic acid showed interactions with inflammatory mediators, TNF and IL6, while phytol was predicted to target DPP4. Squalene exhibited interaction with MAPK1. The targets are linked to glucose metabolism, inflammatory signalling, regulation of oxidative stress and insulin resistance.

**Figure 3 :VENN Diagram of Target prediction**




### 3.4 Identification of Diabetes Mellitus-Associated Genes

Genes associated with diabetes were collected from the GeneCards, OMIM and DisGeNET databases. The major genes identified were AKT1, PPARG, TNF, IL6, PIK3CA, INS, MAPK1, IRS1, DPP4 and SLC2A4. These genes are there in critical roles for insulin signalling, inflammatory response, glucose transport, oxidative stress, and diabetic complications.

### 3.5 Venn Analysis of Overlapping Targets

To determine common targets between the proteins predicted by the phytocompounds and the diabetes mellitus associated genes, venn analysis was carried out. The results indicated that common targets such as AKT1, PPARG, TNF, IL6, PIK3CA, DPP4, and MAPK1 were identified. Such common targets were regarded as being potential therapeutic targets involved in the antidiabetic activity of *Ricinus communis* phytoconstituents.

### 3.6 Protein–Protein Interaction Network Analysis

Protein–protein interaction (PPI) analysis was carried out using STRING database and represented using Cytoscape software. The network showed robust interconnections between the targets identified, suggesting that insulin signalling, inflammatory pathways and glucose metabolism are co-regulated. The network analysis identified the following hub genes: AKT1, PPARG, TNF, IL6 and PIK3CA. PIK3CA and AKT1 are key regulators of PI3K–AKT pathway which regulate glucose uptake and insulin sensitivity and the inflammatory cytokines TNF and IL6 are involved in insulin resistance. PPARG is essential in the regulation of lipid metabolism and adipocyte differentiation.

(ISSN: 0973-7049(P))

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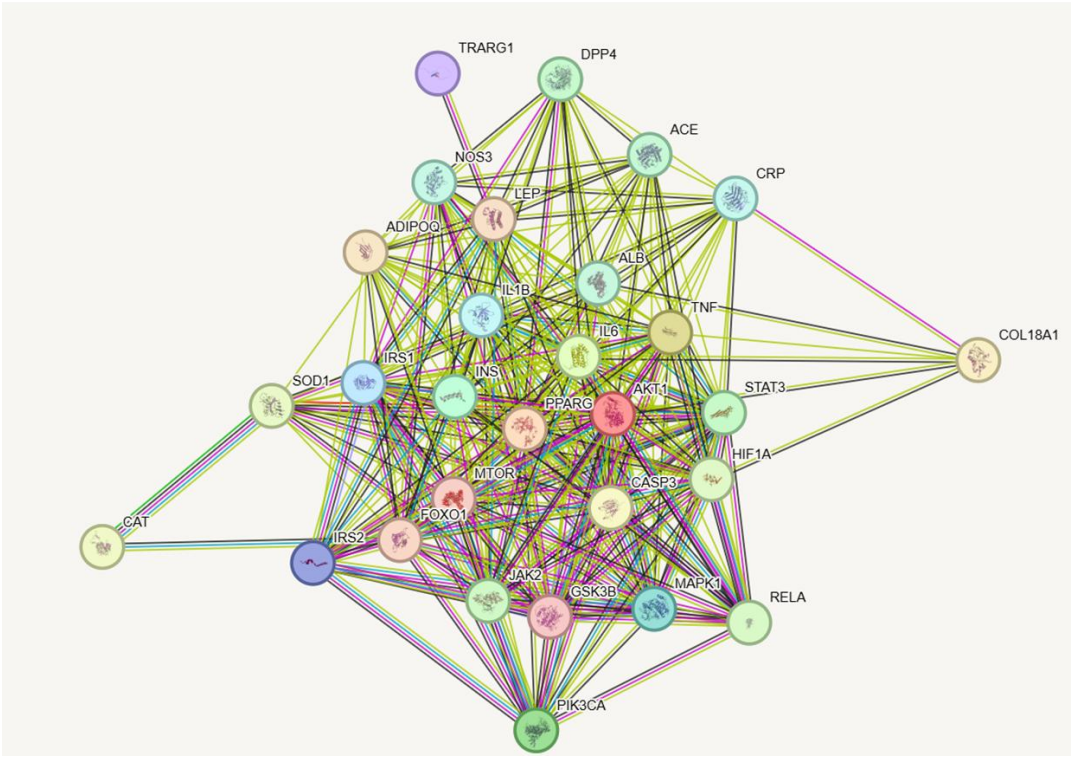
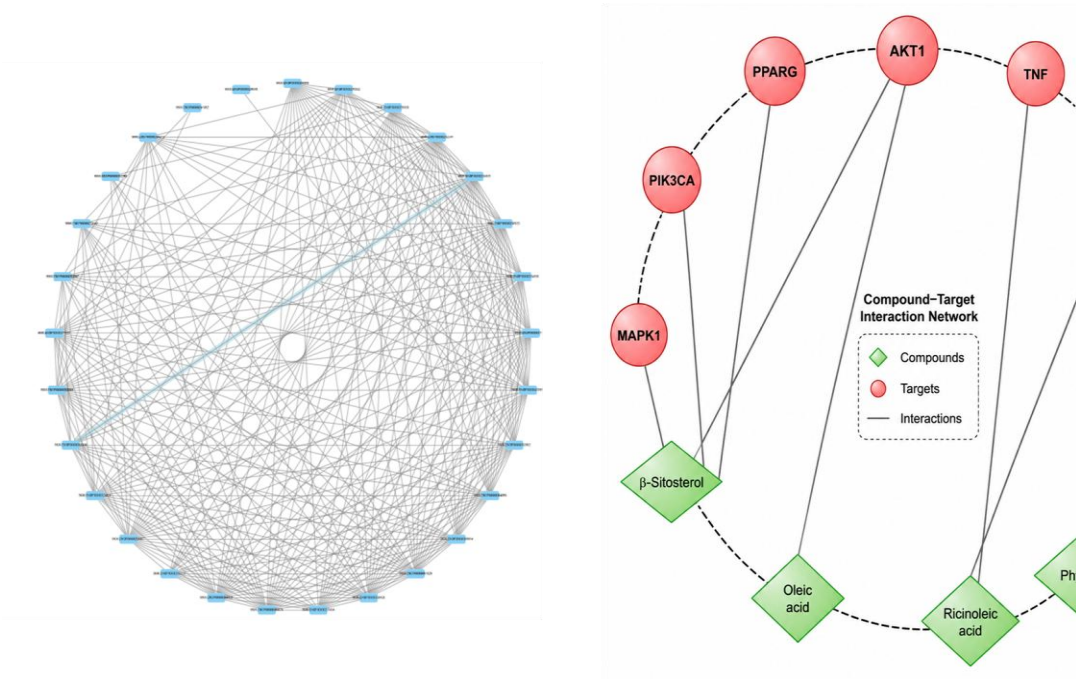
**Figure 4: STRING analysis of Protein-Protein interaction**




### 3.7 Compound–Target Interaction Network Analysis

The compound–target interaction network analysis uncovered the presence of multiple interactions between identified phytocompounds and the proteins associated with diabetes, for example: β-Sitosterol had multiple interactions with PPARG and AKT1, while oleic acid had multiple interactions with AKT1 and PIK3CA. The associations seen for ricinoleic acid were to TNF and IL6, while phytol was seen to interact with DPP4, and squalene interacted with MAPK1. The network hypothesized that the phytoconstituents could have a synergistic antidiabetic effect by acting on multiple pathways associated with insulin action, inflammation, glucose transport and oxidative stress response.

**Figure 5:Ligand –Protein interaction**



### 3.8 Functional Enrichment and Pathway Analysis

Functional enrichment analysis by Metascape revealed enrichments of diabetes mellitus associated biological pathways. Some major enriched pathways were the PI3K–AKT signalling pathway, AGE-RAGE signalling pathway in diabetic complications, leptin signalling pathway, inflammatory response pathways and oxidative stress-related pathways. Biological process analysis showed enrichment of cellular response to peptide hormone stimulus, regulation of inflammatory response, response to oxidative stress and glucose metabolic processes. The results of the enrichment bear out the involvement of identified phytocomponents in insulin sensitization, regulation of glucose uptake, inflammation regulation and protection against diabetic complications.

**Figure (6). Metascape -Based Functional Enrichment and Protein Interaction Network Analysis of Candidate Target Genes**

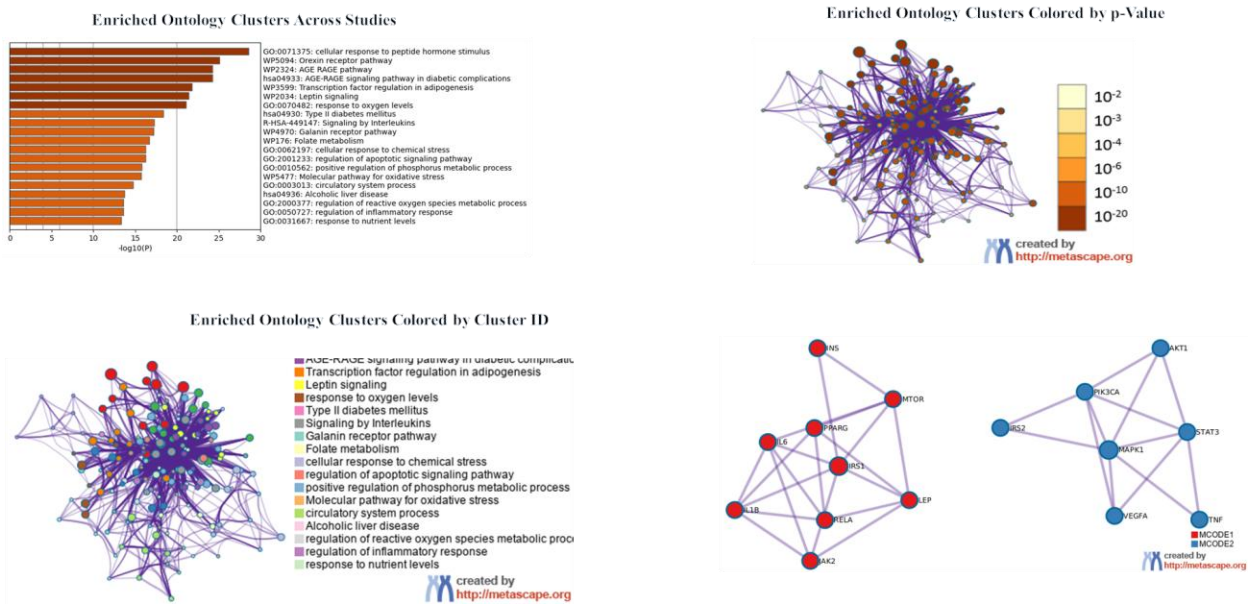
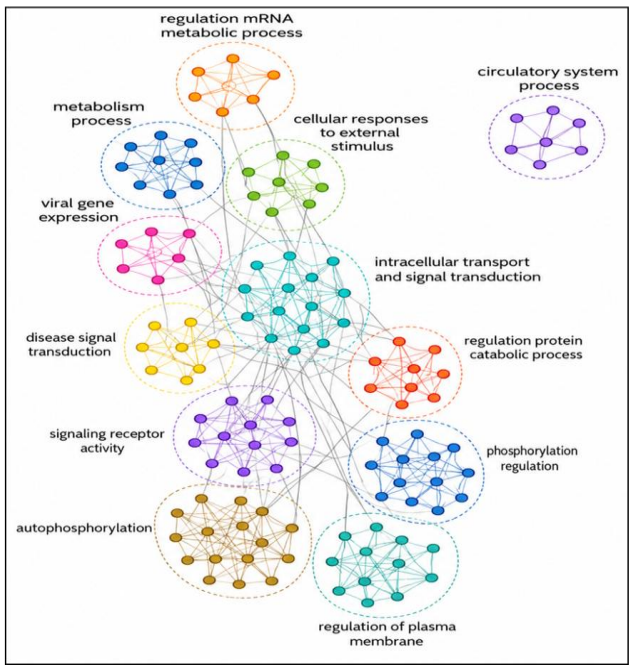


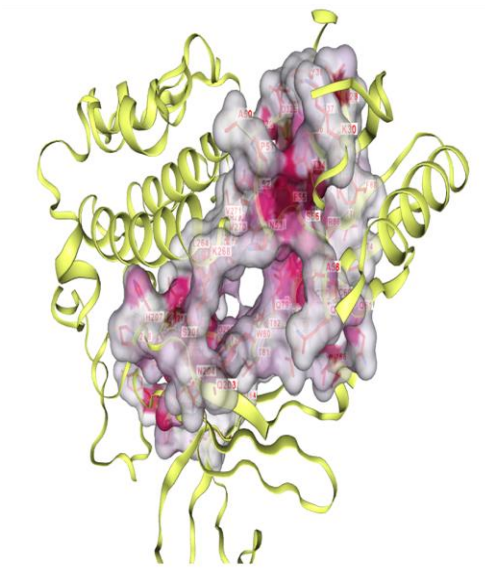

**Figure (7) Gene Ontology Biological Process (GO-BP) Enrichment Network of Common Target Genes**




### 3.9 Molecular Docking Analysis

The molecular docking analysis revealed that selected phytocompounds had strong binding affinity with major target proteins in antidiabetic condition, wherein β-Sitosterol showed significant binding with PPAR-γ suggesting its potential role as insulin sensitizer and glucose metabolism regulator. Ricinoleic acid showed good interactions with α-glucosidase indicating inhibitory activity against carbohydrate digestion and glucose absorption. The binding stability of oleic acid to AKT1 and that of phytol to DPP4 were also found to be stable. Supporting the therapeutic potential of the selected phytocompounds were the hydrogen bonds, hydrophobic contacts and docking scores.

**Figure (8) Active Site prediction of AKT**



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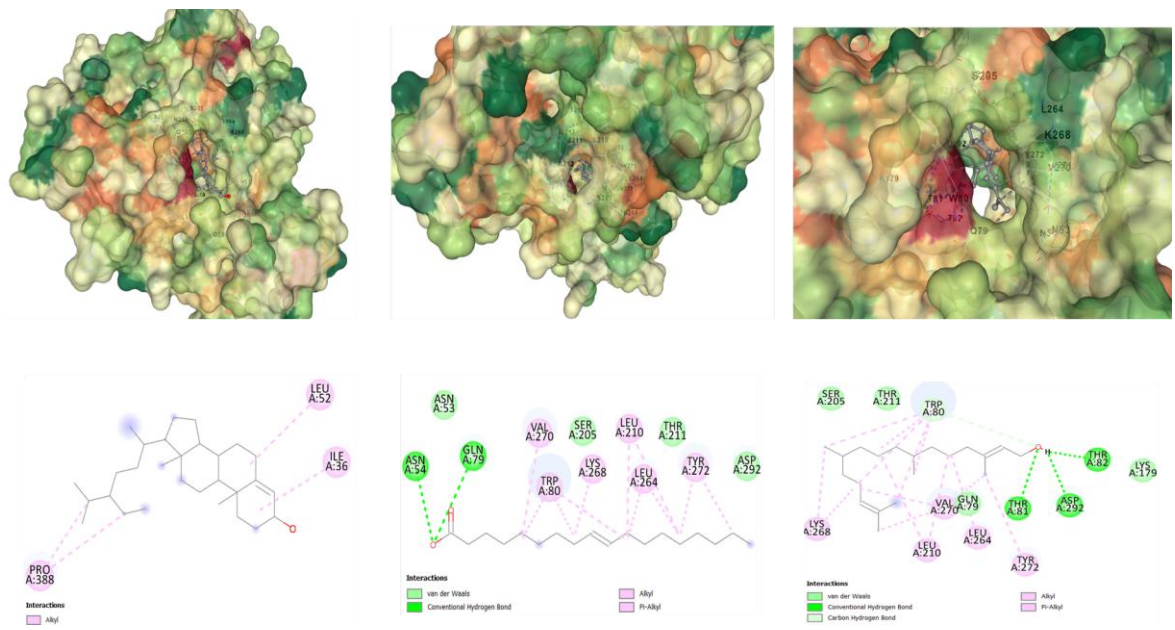
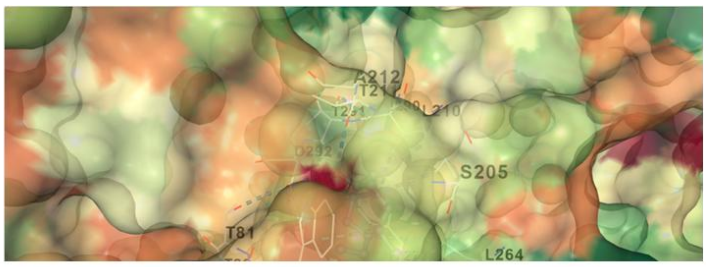
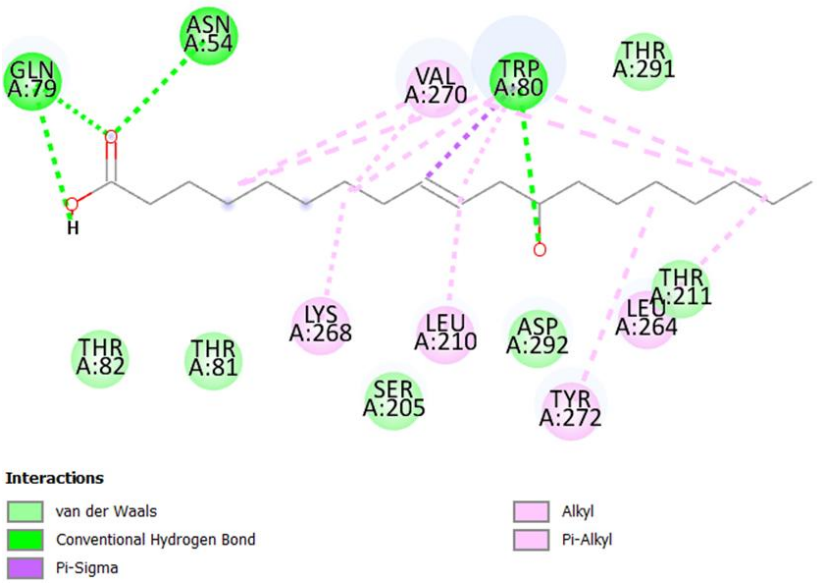
14:K:A,15:R:A,16:G:A,17:E:A,18:Y:A,20:K:A,21:T:A,22:W:A,27:F:A,28:L:A,30:K:A,34:T:A,36:I:A,37:G:A,38:Y:A,50:A:A,51:P:A,52:L:A,53:N:A,54:N:A,55:F:A,56:S:A,58:A:A,59:Q:A,60:C:A,61:Q:A,74:I:A,76:R:A,77:C:A,78:L:A,79:Q:A,80:W:A,81:T:A,82:T:A,83:V:A,84:I:A,85:E:A,86:R:A,87:T:A,88:F:A,154:K:A,156:L:A,157:G:A,161:F:A,164:V:A,166:L:A,186:I:A,203:Q:A,204:N:A,205:S:A,207:H:A,208:P:A,210:L:A,211:T:A,212:A:A,229:Y:A,233:G:A,234:E:A,237:F:A,264:L:A,268:K:A,270:V:A,271:V:A,272:Y:A,273:R:A,274:D:A,276:K:A,278:E:A,279:N:A,281:M:A,289:K:A,290:I:A,291:T:A,292:D:A,293:F:A,294:G:A,295:L:A,296:C:A,297:K:A,298:E:A,299:G:A,308:T:A,309:F:A,310:C:A,311:G:A,312:T:A,316:L:A,320:V:A,323:D:A,324:N:A,325:D:A,326:Y:A,358:F:A,437:Y:A,438:F:A2 482 39.855 58.945 5.852 10 15 8
174:R:A,175:Y:A,176:Y:A,208:P:A,209:F:A,228:E:A,229:Y:A,230:A:A,231:N:A,283:D:A,284:K:A,288:I:A,289:K:A,419:K:A,432:E:A,433:T:A,438:F:A3 224 37.149 27.007 15.145 14 7 6
319:E:A,324:N:A,325:D:A,326:Y:A,327:G:A,328:R:A,329:A:A,388:P:A,393:G:A,394:G:A,395:G:A,398:D:A4 121 35.337 53.639 25.909 5 10 4 78:L:A,80:W:A,202:L:A,216:S:A,217:F:A,223:L:A,224:C:A,225:F:A5 120 23.538 61.047 22.740 7 8 6 147:M:A,162:G:A,163:K:A,180:I:A,182:K:A,219:T:A,222:R:A,224:C:A



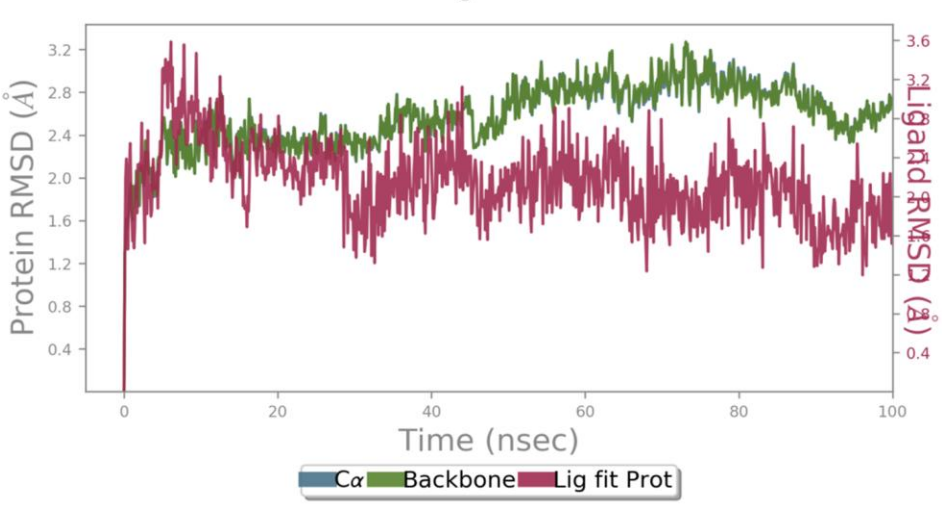


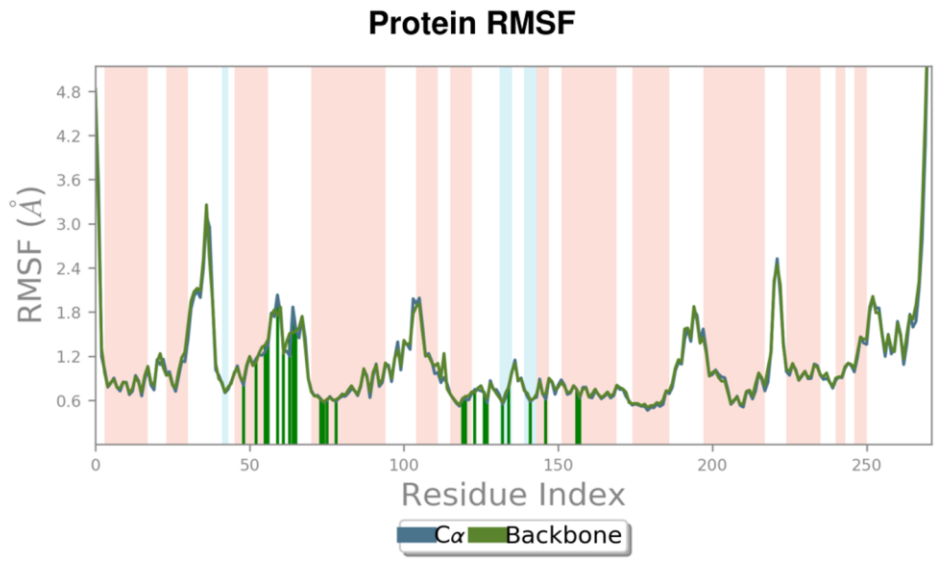




### 3.10 Molecular Dynamics Simulation Analysis

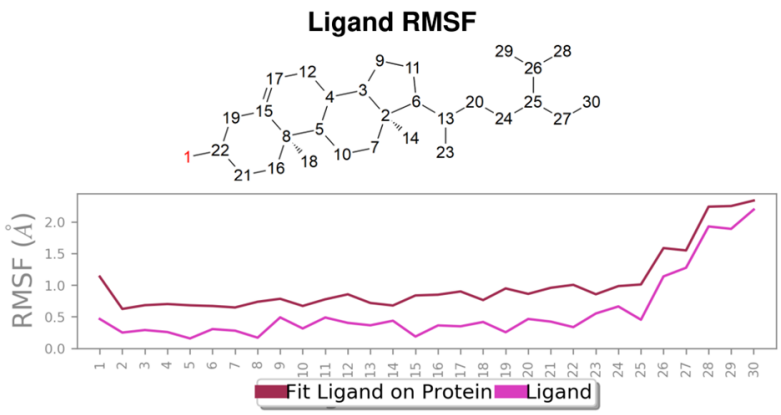
The molecular dynamics simulation studies were carried out to assess the stability of the selected protein–ligand complexes. The RMSD profile of the complexes formed by β-sitosterol–PPAR-γ and ricinoleic acid–α-glucosidase were found to be stable throughout the simulation, which suggested that the protein–ligand interactions remained constant under physiological conditions.

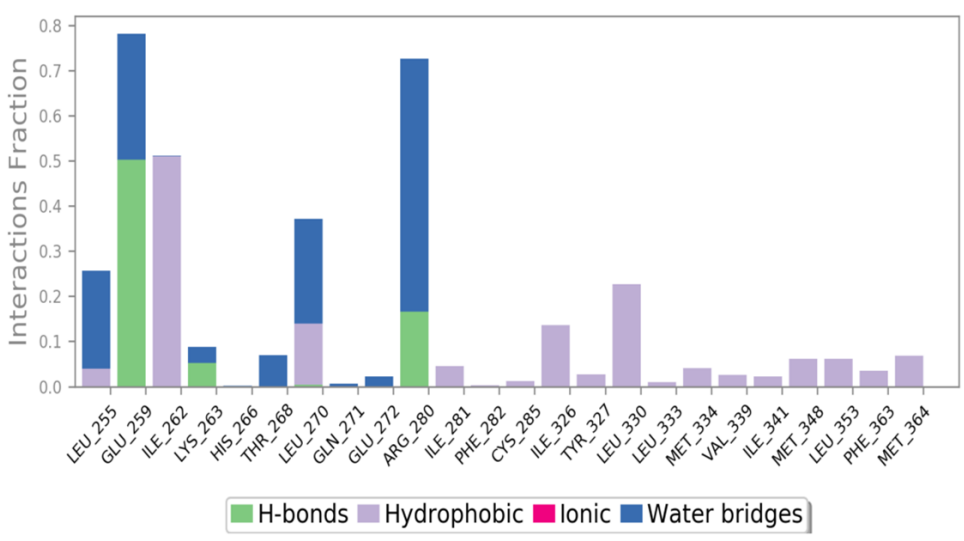
**Figure (11) Molecular Dynamics Simulation -β-Sitosterol – PPARγ Complex**

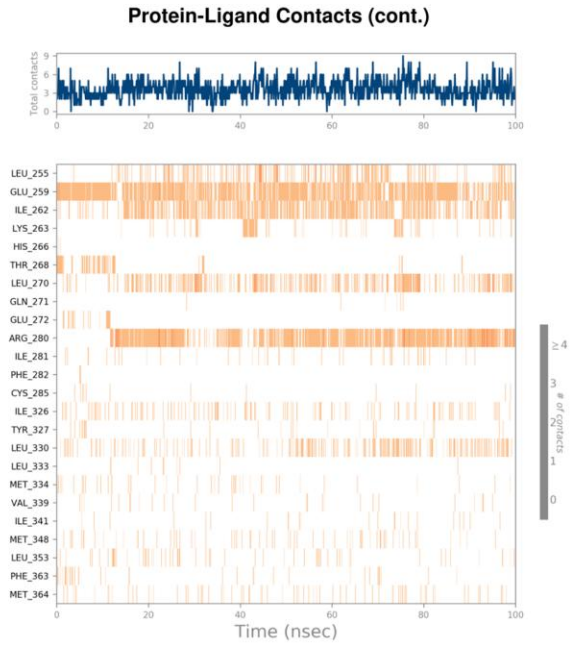


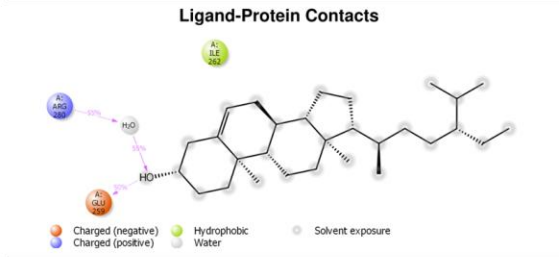

Protein RMSF
RMSF (Å)
Residue Index
Cα
Backbone

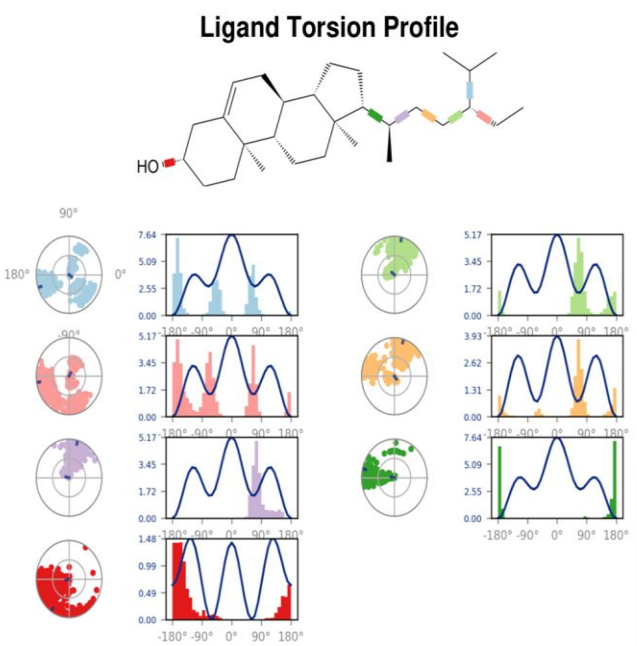

Protein Secondary Structure
% Helix
54.06
% Strand
4.10
% Total SSE
58.16
Res. % SSE
Residue Index

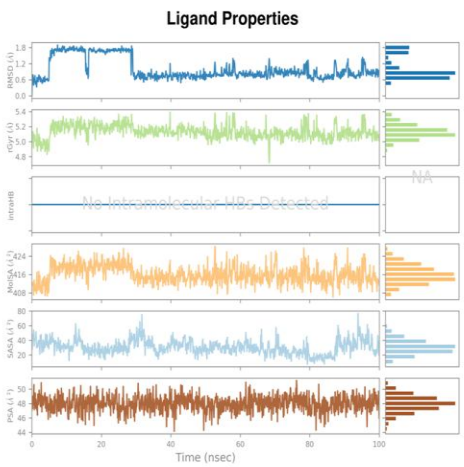

Ligand RMSF
RMSF (Å)
Fit Ligand on Protein
Ligand


Protein-Ligand Contacts
Interactions Fraction
LEU_255
GLU_259
ILE_262
LYS_263
HIS_266
THR_268
LEU_270
GLN_271
GLU_272
ARG_280
ILE_281
PHE_282
CYS_285
ILE_326
TYR_327
LEU_330
LEU_333
MET_334
VAL_339
ILE_341
MET_348
LEU_353
PHE_363
MET_364
H-bonds
Hydrophobic
Ionic
Water bridges




## 4.0 Discussion

The antidiabetic activity of the phytoconstituents in the leaves of Ricinus communis was studied using an integrated phytochemical and computer approach. GC–MS revealed the presence of several biologically active compounds such as β-sitosterol, oleic acid, ricinoleic acid, phytol, squalene and caryophyllene, all of which have antioxidant, anti-inflammatory, hypoglycemic and metabolic regulatory properties (Al-Snafi et al., 2020). The abundance of these compounds is represented by the peak intensity of β-sitosterol that may play a major contribution to the observed pharmacological effects (Bao et al., 2022).

In the past, it has been reported that phytosterols like β-sitosterol have beneficial effects on glucose metabolism and insulin sensitivity via activation of pathways involving PPAR-γ (Sarkar et al., 2026). Oleic acid has been linked to improvement of insulin signalling by regulating PI3K–AKT pathways, whilst ricinoleic acid is also known to have

anti-inflammatory effect via the regulation of the signalling pathways in TNF and IL6 (Santa-Maria et al. 2023). Their appearance in the present GC–MS profile strongly suggests the therapeutic implication of Ricinus communis for diabetes.

Based on SwissADME analysis, most of the selected compounds possessed favourable pharmacokinetic and drug-like properties, such as oleic acid, ricinoleic acid, phytol and β-sitosterol (Jagtap et al., 2025). The result of bioavailability radar revealed their good gastrointestinal absorption, flexibility, polarity, and lipophilicity, which mean they may be orally active therapeutic agents (Simsek, et al 2026). The relative lipophilic properties of β-sitosterol may be useful to improve receptor binding affinity and membrane permeability, whereas its low aqueous solubility might be useful to increase its bioavailability.

The network pharmacology analysis revealed that the phytocompounds identified have several targets interactions with proteins associated with diabetes (Anand et al., 2025). The compound–target interaction network showed that, β-sitosterol targeted to the receptor PPARG and oleic acid targeted to AKT1 and PIK3CA ( Zhang et al., 2025). Enayati et al., 2022, concluded that ricinoleic acid was associated with inflammatory mediators TNF and IL6, respectively, and phytol and squalene were associated with DPP4 and MAPK1, respectively. These results suggest that the phytoconstituents can have synergistic therapeutic effects acting on insulin signalling, inflammatory regulation, oxidative stress response and glucose metabolic pathways all at once.

The protein–protein interaction analysis showed that there were high scores for AKT1, PPARG, TNF, IL6 and PIK3CA, the major hub genes. AKT1 and PIK3CA are key components in the PI3K–AKT glucose uptake and insulin sensitivity pathway, and PPARG is responsible for adiposeness and lipid metabolism (Solinas et al., 2022). The inflammatory cytokines, such as TNF and IL6, are significantly involved with insulin resistance and chronic diabetic inflammation. The highly interconnected PPI network suggests that inflammatory and metabolic pathways are involved in the progression of diabetes, being regulated in a coordinated manner (Norzagaray et al., 2025).

These observations were further substantiated by functional enrichment analysis which revealed significant enrichment of pathways involved in PI3K-AKT signaling pathway, AGE–RAGE signaling pathway in diabetic complications, leptin signalling pathway, oxidative stress response and inflammatory signaling pathways (Suriyagandhi et al., 2022). The AGE–RAGE pathway has been well documented to be involved in hyperglycemia-induced oxidative damage and diabetic complications. Hence, the ability to modulate these pathways by Ricinus communis phytoconstituents can help improve glucose homeostasis and prevent diabetic tissue damages (Raghav et al 2022).

Molecular docking analysis results indicated that β-sitosterol had higher binding affinity towards the PPAR-γ and ricinoleic acid has a higher binding affinity towards α-glucosidase with the potential to increase insulin sensitivity and carbohydrate digestion inhibition (Lolok, N et al., 2022). The interaction between the ligands and the receptors was found to be strong due to stable hydrogen bonding, hydrophobic interaction and positive docking scores. Moreover, the stability of the β-sitosterol-PPARγ complex in the 100 ns simulation time was confirmed by the MD simulation studies. The RMSD of the protein–ligand structures remained below 2-3 Å during the 200-ns simulation and showed to be satisfactory as the system was equilibrated and maintained a stable protein–ligand interaction throughout the simulation (Amanat et al., 2025).

The RMSF analysis revealed that the variations were relatively small in most of the protein residues while at the loop regions at the ends, only small variations were observed; this indicates that the protein backbone is quite rigid during the simulation. The total secondary structure elements were found to be about 58.16% for the whole simulation period by secondary structure analysis and showed stability of the protein structure on binding with the ligand (Alagesan et al 2026). Protein–ligand contact analysis also revealed the stable binding of β-sitosterol in the binding pocket area where the residues GLU259, ARG280 and ILE262 formed persistent hydrophobic contacts and hydrogen bonds with the β-sitosterol.

The torsion profile analysis and the analysis of the properties of the ligand revealed that the conformation of the ligand during the simulation was flexible and the molecular compactness of the ligand was stable. Overall, the results of the molecular dynamics strongly suggest that the docking results are reliable, and that the structure of the complex between β-sitosterol and PPARγ is stable under physiological conditions (Otuokere et al., 2026).

In summary, present study indicates that phytoconstituents of Ricinus communis could be beneficial in controlling diabetes due to multiple targets modulation of insulin signalling pathways, inflammatory mediators, oxidative stress pathways and glucose metabolic processes. The mechanism of action of Ricinus communis and identification of the lead compound was elucidated using integrated network pharmacology, molecular docking, and molecular dynamics simulation approach and the identified lead compound was β-sitosterol, which could be used as a potential lead compound for developing new antidiabetic drugs (Chakraborty et al., 2026).

**Conclusion**

The findings from the present study revealed that the phytoconstituents of Ricinus communis leaves possess antidiabetic properties when subjected to integrated approach namely, phytochemical methods and computational methods. GC–MS analysis identified a number of biologically active compounds including β-sitosterol, oleic acid, ricinoleic acid, phytol and squalene with metabolic, antioxidant and anti-inflammatory properties. Based on SwissADME evaluation the selected compounds exhibited favourable pharmacokinetic and drug-likeness properties, aiding their aptitude for further drug development. The done important diabetes associated targets such as AKT1, PPARG, TNF, IL6, PIK3CA, DPP4 and MAPK1 were identified by network pharmacology analysis, indicating the multi-target role of the phytoconstituents identified. The protein–protein interaction and enrichment analyses also revealed that the compounds of Ricinus communis were involved in PI3K–AKT signalling pathway, AGE–RAGE signalling pathway, inflammatory pathways, oxidative stress regulation, and glucose metabolism pathways.

Based on the result of molecular docking, β-sitosterol is capable to bind to PPAR-γ with high binding affinity and ricinoleic acid can bind to α-glucosidase with high binding affinity. The structural stability and favourable interaction of the complex of the β-sitosterol-PPARγ in physiological conditions were also confirmed by molecular dynamics simulation. In summary, the results indicate that the phytoconstituents of Ricinus communis leaves hold great potential for their antidiabetic effects, mediated by a combination of insulin signalling, inflammatory mediators, oxidative stress pathways, and metabolic regulation. Amongst the identified compounds β-sitosterol was found to be a promising lead compound for further studies to develop the drugs for diabetes. Based on the present study, it can be concluded that Ricinus communis can be used

in traditional medicine to treat diabetes mellitus and the integration of GC–MS analysis, network pharmacology, molecular docking and molecular dynamics simulation is important in finding plant-derived therapeutic agents for diabetes mellitus.

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