Jurnal Masyarakat Informatika, 16(2), 2025
DOI:10.14710/jmasif.16.2.73574
ISSN: 2777-0648

Artificial Intelligence-Aided In Silico Screening of *Syzygium polyanthum* Phytochemicals for Antidiabetic Drug Discovery Using ACO (Ant Colony Optimization) Algorithm

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Abstract

This research employs an artificial intelligence (AI)-driven molecular docking approach to identify potential antidiabetic compounds from Syzygium polyanthum phytochemicals targeting the α-glucosidase enzyme. The docking simulations were conducted using the PLANTS software, which utilizes an ant colony optimization (ACO) algorithm, a nature-inspired AI technique that mimics the foraging behavior of ants to explore ligand binding conformations efficiently. PLANTS integrates multiple empirical scoring functions, including ChemPLP, to evaluate protein-ligand interactions by modeling steric complementarity, hydrogen bonding, and torsional potentials, enabling accurate prediction of binding affinities. The protein structure with PDB code 2JKE was validated with a root-mean-square deviation (RMSD) of 0.2912 Å, confirming the reliability of the docking protocol. Screening results revealed seven phytochemical compounds Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl), Methyl oleate, Methyl palmitate, Phytol, 9,12,15-Octadecatrien-1-ol, Nerolidol, and Eicosane exhibited lower docking scores (-96.2919 to -80.5188) than both the reference drug miglitol (-80.2642) and the native ligand (-77.2910), indicating stronger and more stable binding to the α-glucosidase active site. These findings suggest that the identified compounds have superior theoretical inhibitory potential compared to miglitol, a clinically used α-glucosidase inhibitor. The AI-based in silico screening using PLANTS thus provides a powerful, cost-effective strategy for accelerating antidiabetic drug discovery by prioritizing promising natural compounds for further experimental validation.

Keywords : *Artificial Intelligence, PLANTS software, Syzygium polyanthum, Antidiabetic Drug*

1 Introduction

Artificial Intelligence (AI)-assisted in silico screening has emerged as a transformative approach in drug discovery, addressing the traditional challenges of time, cost, and complexity inherent in developing new therapeutics [1]. Conventional drug discovery methods often rely on labor-intensive, trial-and-error experimentation and high-throughput screening, which are time-consuming and expensive. AI technologies, particularly machine learning (ML) and deep learning (DL), have

Received: 23 May 2025; Revised: 8 July 2025; Accepted: 14 July 2025; Published: 18 July 2025

revolutionized this landscape by enabling the rapid analysis of vast chemical and biological datasets, facilitating the identification and optimization of potential drug candidates with greater efficiency and accuracy [2].

In silico screening, encompassing both ligand-based and structure-based virtual screening, leverages computational models to predict the binding affinity and biological activity of compounds against target proteins [3]. AI enhances these methods by improving the prediction of pharmacological properties, ADMET (absorption, distribution, metabolism, excretion, and toxicity) profiles, and drug-target interactions, thereby increasing the success rate of candidate selection and reducing reliance on costly laboratory assays [4]. The integration of AI-driven techniques allows for ultra-high-throughput screening and the exploration of novel chemical spaces, including the de novo design of drug-like molecules that may not be accessible through traditional chemistry [5].

Molecular docking-assisted in silico screening has emerged as a pivotal technique in modern drug discovery due to its ability to predict and analyze the interactions between small molecules (ligands) and biological targets (proteins or receptors) at the atomic level [6]. This computational approach enables researchers to virtually screen vast libraries of compounds to identify potential drug candidates by estimating their binding affinity and mode of interaction with target proteins, thereby significantly accelerating the early stages of drug development [7]. The structure-based nature of molecular docking relies on high-resolution three-dimensional representations of target proteins, obtained through experimental methods such as X-ray crystallography or cryo-electron microscopy, which enhances the accuracy of docking predictions [8]. Molecular docking facilitates hit identification by enabling the rapid evaluation of numerous compounds, thus prioritizing those with the highest likelihood of efficacy before costly and time-consuming experimental testing [9]. Beyond initial screening, docking also supports lead optimization by predicting how chemical modifications of a molecule might improve binding affinity and selectivity, guiding rational drug design [10].

Molecular docking software has increasingly adopted advanced metaheuristic algorithms such as Ant Colony Optimization (ACO), Particle Swarm Optimization (PSO), and Genetic Algorithms (GA) to enhance the accuracy and efficiency of virtual screening in drug discovery. Notably, the PLANTS docking program utilizes the ACO algorithm to explore ligand binding poses, offering features like multiple scoring functions and explicit modeling of water molecules [11]. For PSO, tools such as pso@autodock and ClustMPSO integrate swarm intelligence to rapidly and flexibly dock highly rotatable ligands, often outperforming traditional methods in speed and solution diversity [12]. Genetic Algorithms are widely implemented in molecular docking platforms like AutoDock and Glide, where they optimize ligand-receptor interactions by mimicking evolutionary processes [13]. The main differences among these algorithms lie in their search strategies: ACO relies on the collective behavior of artificial ants to find optimal paths based on pheromone trails, PSO simulates the social behavior of particles adjusting their positions based on individual and group experiences, while GA employs selection, crossover, and mutation to evolve populations toward optimal solutions [14]. ACO offers a critical advantage in local searching and solution refinement, often achieving higher accuracy and robustness in complex search spaces compared to PSO and GA, which can be more prone to premature convergence or require more computational resources for global exploration [15]. This makes ACO particularly valuable for molecular docking tasks that demand precise identification of binding conformations in large and intricate chemical spaces.

The search for antidiabetic drugs remains an active and critical area of research due to the increasing global prevalence of diabetes mellitus and the limitations of current therapies. Despite the availability of conventional antidiabetic drugs such as insulin and oral agents (e.g., sulfonylureas, biguanides), these treatments often have significant side effects and may not fully prevent the chronic complications associated with diabetes [16]. Consequently, there is a continuous need to discover safer, more effective, and affordable antidiabetic agents.

In this study, the Ant Colony Optimization (ACO) algorithm employed for in silico phytochemical screening is a bio-inspired metaheuristic that mimics the foraging behavior of ants to solve combinatorial optimization problems by finding optimal paths on a weighted graph. The core mechanism involves artificial ants stochastically constructing candidate solutions (paths) based on pheromone trails and heuristic information, followed by pheromone updating to reinforce promising solutions and guide subsequent searches. Key parameters include the number of ants mm, pheromone importance factor αα, heuristic desirability factor ββ, pheromone evaporation rate ρρ, and pheromone deposit quantity QQ, which collectively balance exploration and exploitation during the search process. Specifically, αα controls the influence of pheromone trails, ββ governs the impact of heuristic information (such as inverse distance or binding affinity), and ρρ prevents premature convergence by simulating pheromone evaporation. Compared to other population-based algorithms like PSO and GA, ACO uniquely leverages indirect communication via pheromone trails, enabling adaptive path construction and efficient solution refinement in discrete search spaces. While PSO emphasizes velocity and position updates based on personal and global bests in continuous spaces, and GA relies on crossover and mutation operators to evolve populations, ACO's iterative pheromone-guided probabilistic solution construction offers advantages in combinatorial problems such as molecular docking and drug candidate selection. Mild modifications in this work include tuning the pheromone evaporation rate and heuristic factors to better capture the chemical interaction landscape of Syzygium polyanthum phytochemicals, enhancing convergence speed and solution quality. This tailored ACO approach thus contributes to informatics by providing a robust, biologically inspired optimization framework well-suited for antidiabetic drug discovery from complex natural product libraries [17].

Medicinal plants have historically been and continue to be a valuable source of potential antidiabetic compounds [18]. Many plants contain diverse bioactive phytochemicals, such as flavonoids, terpenoids, saponins, alkaloids, glycosides, and polyphenols that exhibit antihyperglycemic properties through various mechanisms, including insulin mimetic effects, enhancement of insulin secretion, inhibition of glucose absorption, and modulation of glucose metabolism. The natural origin of these compounds often implies fewer side effects and better patient tolerability, making plant-derived agents particularly attractive, especially in developing countries where access to conventional drugs may be limited [19]. However, the complexity of plant extracts and the need to identify specific active molecules require advanced methods for screening and characterization.

Molecular docking has emerged as a powerful computational technique in the search for new antidiabetic drugs, especially for screening plant-derived compounds [20]. This method simulates the interaction between small molecules (ligands) and target proteins involved in diabetes pathophysiology, such as the alpha-glucosidase enzyme. By predicting the binding affinity and orientation of compounds within the active sites of these proteins, molecular docking helps identify

promising candidates that may modulate key biochemical pathways related to glucose homeostasis and insulin sensitivity [21]. Driven by a desire to combat diabetes, this study explores the potential of compounds within *Syzygium polyanthum*, harnessing the power of molecular docking to identify promising antidiabetic drug candidates. The novelty of this research lies in its integration of Artificial Intelligence techniques with in silico screening specifically focused on *Syzygium polyanthum* phytochemicals for antidiabetic drug discovery.

2 Research Methods

2.1 Tools and Materials

The tools used are Software PLANTS (http://www.tcd.uni-konstanz.de/research/plants.php), ChemAxon (http://www.chemaxon.com/marvin/download-user.html), YASARA (http://www.yasara.org/viewdl.html), Discovery Studio Visualizer (https://www.3ds.com/products/biovia/discovery-studio/visualization), and a 64-bit laptop set.

The material to be used is the protein structure downloaded via https://www.rscb.org/ with PDB code: 2JKE. The test ligand that will be used in the study is the active compound from *Syzygium polyanthum* leaves, and the comparator ligand is miglitol.

2.2 Research Procedure

2.2.1 Protein and Ligand Preparation

First, the crystal structure of the target protein (PDB ID: 2JKE) is retrieved from the Protein Data Bank. The protein structure is prepared by removing water molecules and any co-crystallized ligands, adding missing hydrogen atoms, and assigning appropriate protonation states to ionizable residues to reflect physiological pH. Energy minimization is performed to relieve steric clashes and optimize the structure for docking. The active site or binding pocket is defined based on either the co-crystallized ligand position or known active site residues [22].

The comparative ligand miglitol and the test bioactive compounds from *Syzygium polyanthum* leaves including 4-allyl-1,2-dihydroxybenzene (hydroxychavicol); Squalene; Phytol; 1H-cyclopropa[a]naphthalene; n-heptanal; Octanal; Heptane; Eicosane; n-pentacosane; Selina-4,11-diene (naphthalene); Propylene glycol; Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl); Methyl oleate; Methyl palmitate; 9,12,15-Octadecatrien-1-ol; α-tocopherol; β-tocopherol; γ-tocopherol; Humulene epoxide II; Pyrogallol; β-sitosterol; Pentadecane, 2,6,10,14-tetramethyl-; Azulene; Farnesol; α-copaene; δ-cadinene; α-cubebene; α-pinene; α-panasinsene; β-panasinsene; α-humulene; β-selinene; 2-isopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (α-selinene); Linalool; Neophytadiene; Nerolidol and Valencene (Ismail et al., 2019) are prepared by generating their 3D structures, assigning correct bond orders, protonation states, and performing energy minimization to obtain stable conformations.

2.2.2 Docking Setup, Execution and Scoring

PLANTS software employs an ant colony optimization (ACO) algorithm to explore ligand conformations within the defined binding site. A grid box encompassing the active site is set to restrict the search space, ensuring efficient sampling of ligand poses. The docking parameters are set to allow flexible ligand conformations, while the protein remains rigid [11].

PLANTS generates multiple ligand poses by recursively sampling ligand conformations and orientations within the binding pocket until convergence to minimum energy conformations is reached. Each pose is evaluated using empirical scoring functions designed specifically for PLANTS, such as PLANTSCHEMPLP and PLANTSPLP, which consider various interaction energies [23].

The docking score S in PLANTS is calculated as a weighted sum of interaction terms, primarily including van der Waals and electrostatic interactions, expressed as:

$$S = \sum_{i,j}(E_{vdW}(r_{ij}) + E_{elec}(r_{ij})) \quad (1)$$

Where $E_{vdW}(r_{ij})$ is the van der Waals energy between atoms i and j at distance r_{ij}, and $E_{elec}(r_{ij})$ is the electrostatic interaction energy. These terms are modeled using Lennard-Jones type potentials and Coulomb's law, respectively, parameterized empirically to reflect binding affinity and pose quality. The scoring function aims to approximate the binding free energy ΔG, ranking ligand poses by their predicted affinity [24]. The docking score provided by PLANTS is a weighted sum of interaction energies, including van der Waals and electrostatic terms, approximating the binding free energy ΔG:

$$\Delta G_{dock} = E_{vdW} + E_{electrostatic} + E_{other} \quad (2)$$

2.2.3 Validation and Analysis

To validate the docking protocol, miglitol is re-docked into 2JKE's binding site to confirm that the predicted pose aligns with known binding modes, assessed by root-mean-square deviation (RMSD) values below 2.0 Å [25]. Subsequently, each bioactive compound from *Syzygium polyanthum* is docked, and their docking scores are compared to miglitol's score to evaluate potential binding affinity and inhibitory activity.

The RMSD is calculated using the equation:

$$RMSD = \sqrt{\frac{1}{N}} \sum_{i=1}^{N}((x_i - x_i')^2 + (y_i - y_i')^2 + (z_i - z_i')^2) \quad (3)$$

Where N is the number of atoms considered, (x_i, y_i, z_i) and $(x_i',y_i',z_i')(x_i',y_i',z_i')$ are the coordinates of the i_i-th atom in the reference and docked ligand, respectively [26]. An RMSD value ≤ 2 Å is generally considered indicative of a valid docking pose [27].

2.2.4 Visualization of docking results

To visualize molecular docking results using BIOVIA Discovery Studio (BDS) software, begin by importing the docking output files, typically containing the protein-ligand complex coordinates. Open the complex structure in the 3D Structure Viewer to examine the overall binding pose. Use the Ligand Explorer tool to analyze detailed interactions between the ligand and the receptor, highlighting hydrogen bonds, hydrophobic contacts, and other non-covalent interactions. Adjust the display settings

to show the protein surface or cartoon representation and the ligand as sticks or spheres for clarity. Employ the Complex Viewer to visualize the entire protein-ligand complex, enabling rotation and zoom to inspect binding sites thoroughly. To enhance understanding of the binding environment, generate an electrostatic potential map on the protein surface, which helps illustrate charge complementarity between ligand and receptor. Surface and volume rendering tools can be used to create detailed, publication-quality images by customizing colors, transparency, and lighting effects. Finally, capture high-resolution screenshots or export images for documentation and publication purposes. This comprehensive visualization procedure facilitates interpretation of docking results by clearly depicting molecular interactions and binding site characteristics, supporting further analysis and presentation of findings in research articles [28].

3 Results and Discussion

In this study, the molecular docking process was integrated as a critical component of the computational modelling system for antidiabetic drug discovery. Molecular docking simulates the interaction between small-molecule ligands and target proteins at the atomic level, allowing for the prediction of binding modes and affinities based on structural complementarity and energetics. This process involves several key steps, namely the capture and preparation of protein and ligand structures, optimization of protein conformations (including energy minimization and determination of protonation states), and removal of non-essential molecules to ensure accurate simulations. Docking algorithms then explore possible ligand orientations and conformations within the binding site, employing scoring functions to estimate binding affinities and rank potential drug candidates. This approach enables high-throughput virtual screening and rational lead optimization, moving beyond mere software application to a systematic computational workflow that models molecular interactions and predicts bioactivity [29].

The Ant Colony Optimization algorithm, which underpins the virtual screening process, exhibits a well-characterized computational complexity. The time complexity of traditional ACO algorithms is generally $O(t \cdot k \cdot n^2)$, where n is the number of nodes (e.g., compounds or molecular states), k is the number of ants (agents), and t is the number of iteration which reflects the convergence rate toward optimal solutions, which is influenced by algorithmic parameters such as pheromone evaporation rate and heuristic factors. The space complexity is typically $O(n^2 + kn)$, accounting for pheromone matrices and agent states. Theoretical analyses have shown that, for certain optimization problems, ACO can achieve runtimes competitive with other metaheuristics, with efficiency depending on problem structure and parameterization [30]. These insights reinforce the suitability of ACO as a scalable and effective approach for in silico drug screening.

The initial phase in molecular docking, known as method validation, is fundamental as it guarantees the dependability and precision of the computational protocol before its application to new compounds or targets [31]. Molecular docking leverages advanced algorithms and artificial intelligence techniques to predict how a small molecule, such as a potential drug, interacts within the binding pocket of a target protein. The accuracy of these predictions is highly contingent on the computational models, AI-driven scoring functions, and parameter settings employed. Through rigorous validation, researchers confirm that the AI-based docking framework can accurately replicate experimentally determined binding poses, such as those obtained from crystallographic data [32]. This

validation acts as a critical quality assurance step, ensuring that the machine learning models and computational heuristics are well-suited for the specific protein-ligand system under investigation. Without this essential step, AI predictions risk being unreliable, leading to false leads that could consume valuable time and computational resources in drug discovery pipelines. The importance of method validation is underscored by its role in establishing trust in AI-generated results, preventing error propagation, and minimizing false positives or negatives during virtual screening [33]. Ultimately, method validation bridges the gap between computational predictions and biological reality, emphasizing that behind every AI-driven data point lies a complex molecular interaction that must be accurately modeled to propel scientific innovation forward.

The RMSD (Root Mean Square Deviation) value obtained from this study is 0.2912 Å, demonstrating the exceptional accuracy of our AI-driven molecular tethering approach in reproducing the ligand binding pose relative to the reference or experimental structure. The molecular docking simulation conducted in this study is considered accurate based on the root mean square deviation (RMSD) criterion, where an RMSD value less than 2 Å is widely accepted as indicative of a reliable docking pose. This threshold reflects that the docked ligand conformation closely matches the experimentally observed binding mode, with minimal deviation, thus validating the docking protocol used. Literature benchmarking confirms that docking results with RMSD ≤ 2 Å correspond to correct predictions in the majority of cases, ensuring the credibility of the simulated ligand-receptor interactions and supporting the validity of subsequent analyses such as binding affinity and interaction profiling. RMSD is a quantitative metric that measures the average distance between corresponding atoms of two superimposed molecular structures, in this case, the predicted tethered ligand and the experimentally determined conformation [34]. A lower RMSD value indicates a closer match, reflecting higher predictive accuracy. In molecular docking and tethering studies, RMSD values below 2.0 Å are widely accepted as indicative of good docking predictions because they suggest that the predicted ligand conformation closely approximates the true binding mode, capturing key molecular interactions essential for biological activity [35]. The integration of advanced AI algorithms in our study enhances the precision of ligand pose prediction by effectively learning complex molecular patterns and optimizing docking conformations beyond traditional methods. This is evident in the remarkably low RMSD value of 0.2912 Å obtained here, underscoring the potential of AI to revolutionize structure-based drug design. The conformational similarity of 1-deoxynojirimycin, as validated by our AI model, is illustrated in Figure 1.

Figure 1 Conformation of 1-deoxynojirimycin Before (Red Color) and After (Yellow Color) Tethered with α-glucosidase Enzyme with RMSD Value of 0.2912 Å

The redocking analysis leveraged advanced computational techniques to elucidate the interaction between 1-deoxynojirimycin and key amino acid residues within the active site of α-glucosidase. By harnessing AI-enhanced molecular docking algorithms, the study systematically and quantitatively

mapped out the critical hydrogen bonding and hydrophobic interactions between 1-deoxynojirimycin and the active site residues of α-glucosidase. The AI-driven approach enabled the precise identification of specific donor–acceptor pairs involved in hydrogen bonds, as well as the spatial arrangement and contribution of non-polar residues to hydrophobic stabilization of the ligand. These interactions, including the distances, orientations, and energetic contributions of each contact, are comprehensively illustrated and annotated in Figure 2. Notably, the residues involved Trp331, Lys467, Glu508, Glu526, and Glu532 for hydrogen bonds, and Ile335, Trp341, Trp397, Val471, and His507 for hydrophobic contacts mirror those reported in crystallographic studies by previous studies [36]. This concordance validates the efficacy of AI-enhanced docking simulations in accurately recapitulating experimentally observed binding modes. The integration of machine learning models and computational docking frameworks enabled rapid and precise prediction of ligand-receptor interactions, demonstrating the potential of AI-driven approaches to complement and extend traditional structural biology methods in drug discovery [37].

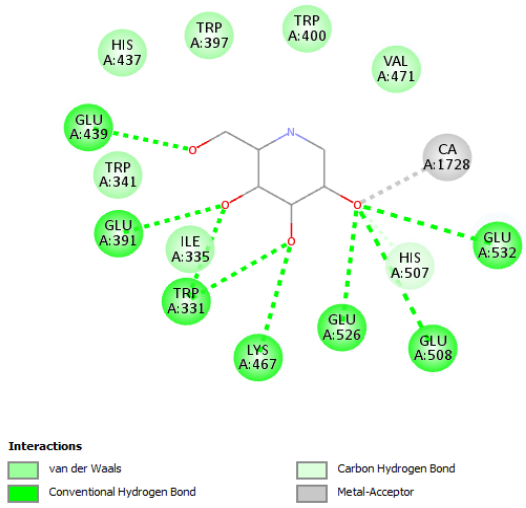


Figure 2 Interaction of 1- deoxynojirimycin with The Active Side of Redocked α-glucosidase

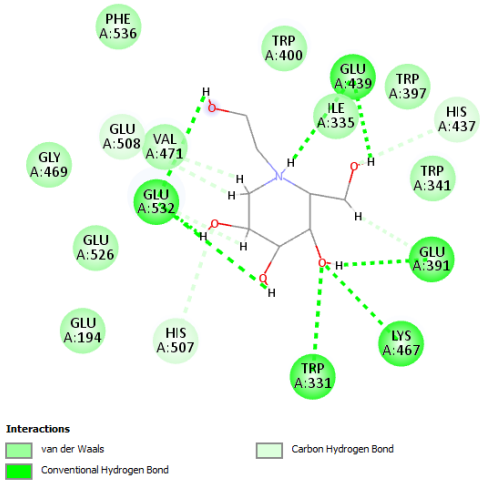
The initial phase of molecular tethering for the selected test compounds was conducted through a comprehensive and advanced computational ligand preparation workflow. This process began with the generation of precise 2D molecular structures for each compound using MarvinSketch software, which allowed for accurate digital representation and manipulation of molecular geometry [38]. Subsequently, protonation states were optimized through the Major Microspecies algorithm, calibrated to physiological pH conditions to reflect the in vivo environment accurately. This optimization step is critical to computationally predict the most biologically relevant conformations that enhance binding affinity to the α-glucosidase receptor [39]. Leveraging AI-driven conformational sampling, ten distinct conformers per compound were algorithmically generated to capture structural diversity. These conformations were then subjected to molecular docking simulations with the target protein, employing scoring functions to quantitatively evaluate binding interactions. These scoring results serve as a predictive measure of each compound's binding affinity and potential biological activity. The outcomes of this docking analysis, including the calculated scores and rankings, are systematically summarized in Table 1.

Table 1 Docking Scores of Test Compounds

No	Test Compounds	Score Docking
1.	Miglitol	-80,26
2.	*Ligand native*	-77,29
3.	*Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)*	-96,29
4.	*Methyl oleate*	-90,59
5.	*Methyl palmitate*	-87,67
6.	*Phytol*	-87,40
7.	*9,12,15-Octadecatrien-1-ol*	-83,27
8.	*Nerolidol*	-81,15
9.	*Eicosane*	-80,52
10.	*Neophytadiene*	-80,23
11.	*Pentadecane, 2,6,10,14-tetramethyl-*	-79,11
12.	*Farnesol*	-76,98
13.	*n-pentacosane*	-75,09
14.	*Linalool*	-70,97
15.	*Squalene*	-68,26
16.	*4-allyl-1,2-dihydroxybenzene (hydroxychavicol)*	-67,36
17.	*Pyrogallol*	-64,76
18.	*2-isopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (α-selinene)*	-62,71
19.	*Valencene*	-61,89
20.	*α-cubebene*	-61,61
21.	*Selina-4,11-diene (naphthalene)*	-61,14
22.	*β-selinene*	-60,81
23.	*Octanal*	-60,41
24.	*δ-cadinene*	-60,20
25.	*β-panasinsene*	-60,18
26.	*α-humulene*	-59,47
27.	*Humulene epoxide II*	-59,17
28.	*α-copaene*	-59,24
29.	*n-heptanal*	-58,24
30.	*α-panasinsene*	-57,20
31.	*Propylene glycol*	-55,50
32.	*1H-cyclopropa[a]naphthalene*	-54,48
33.	*α-pinene*	-53,74
34.	*γ-tocopherol*	-50,54
35.	*Azulene*	-50,53
36.	*β-sitosterol*	-50,088
37.	*Heptane*	-49,43
38.	*β-tocopherol*	-49,41
39.	*α-tocopherol*	-48,88

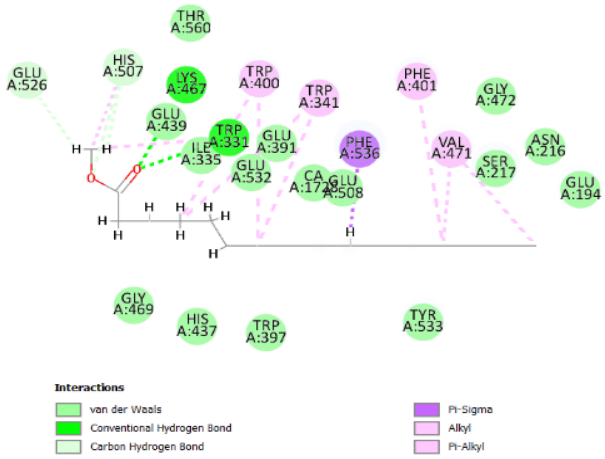
Based on the computational docking results presented in Table I, the compounds Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl), Methyl oleate, Methyl palmitate, Phytol, 9,12,15-Octadecatrien-1-ol, Nerolidol, and Eicosane exhibit docking scores of -96.29, -90.59, -87.67, -87.40, -83.27, -81.15, and -80.52, respectively. These values are notably lower than those of the comparator miglitol (-80.26) and the native ligand (-77.29), indicating stronger predicted binding affinities with the α-glucosidase

enzyme. The docking score, derived from AI-enhanced molecular docking simulations, quantitatively reflects the stability of the ligand-enzyme complex, where a lower score corresponds to a more stable and energetically favorable interaction. This AI-driven docking approach leverages advanced machine learning algorithms to efficiently explore ligand conformations and binding poses, accelerating the identification of promising inhibitors by predicting binding strength with high accuracy and speed. Thus, the enhanced binding stability observed for these compounds suggests their potential as effective α-glucosidase inhibitors, as revealed through state-of-the-art artificial intelligence-powered virtual screening methodologies [40]. Visualization of docking results performed using Discovery Studio Visualizer software for 2D amino acid interactions of miglitol, Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl) Methyl oleate, Methyl palmitate, Phytol, 9,12,15-Octadecatrien-1-ol, Nerolidol, and Eicosane are presented in Figure 3.



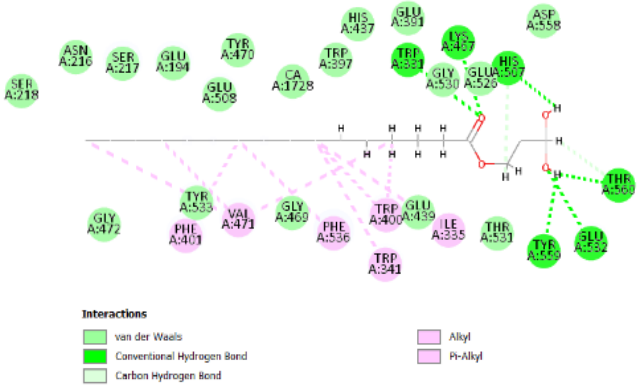
Miglitol 2D

(a)



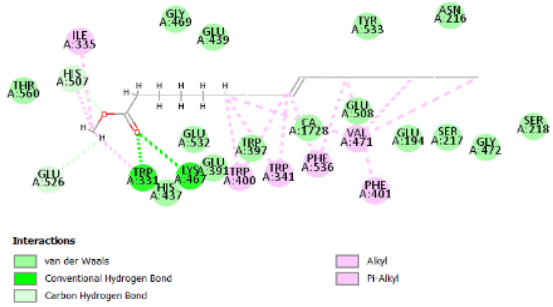
Methyl Palmitate 2D

(b)



Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) 2D

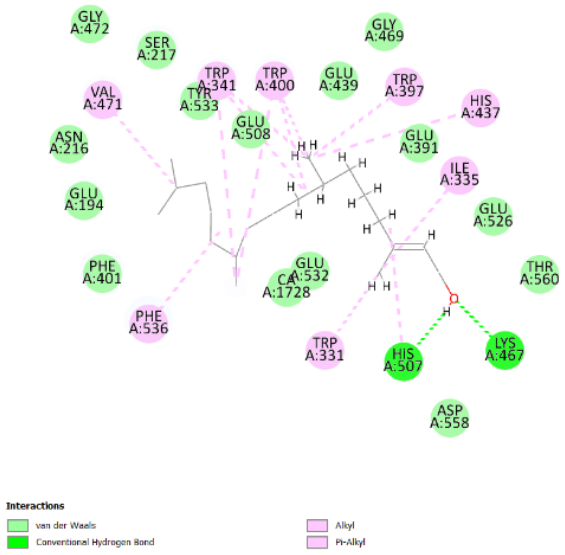
(c)



Methyl Oleate 2D

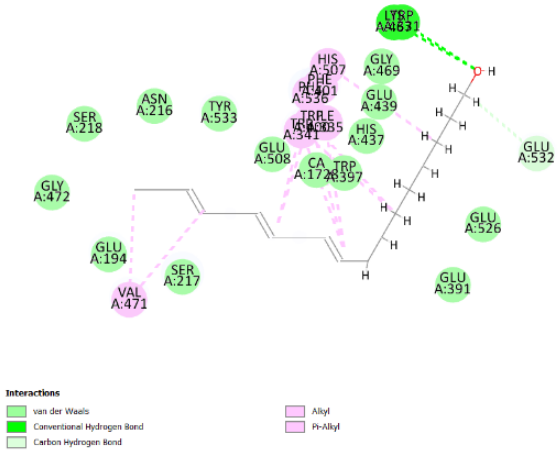
(d)

Figure 3. Visualization of docking results (a) Miglitol, (b) Methyl palmitate, (c) 2-hydroxy-1-(hydroxymethyl) hexadecanoic acid, (d) Methyl oleate



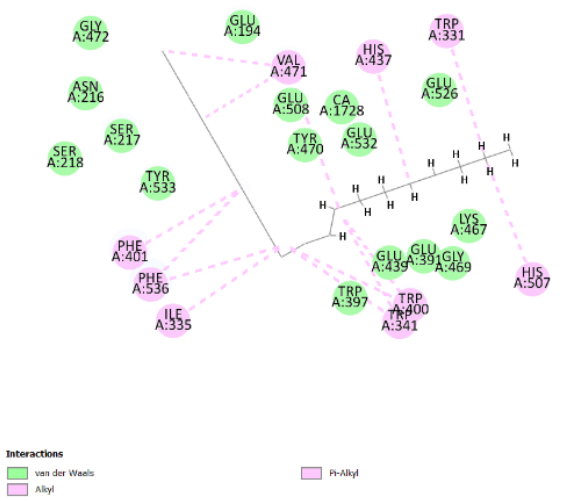
Phytol 2D

(e)



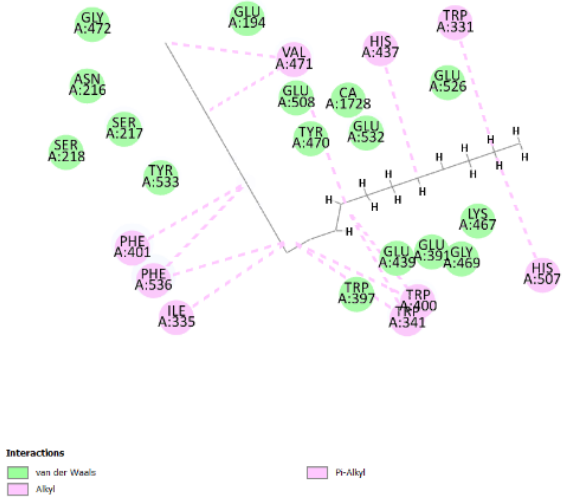
9,12,15-Octadecatrien-1-ol 2D

(f)



Nerolidol 2D

(g)



Eicosane 2D

(h)

Figure 3. (contd.) (e) Phytol, (f) 9,12,15-Octadecanoic-1-ol, (g) Nerolidol and (h)Eicosane

Based on the computational visualization in Figure 3, ligand-receptor interactions are distinctly color-coded to represent various atomic and bonding features, facilitating clear differentiation of interaction types in silico. This color scheme highlights van der Waals interactions (light green), conventional hydrogen bonds (dark green), and hydrophobic interactions such as pi-alkyl and alkyl bonds (light purple), which are critical for understanding molecular docking dynamics. The use of advanced molecular docking algorithms enables the quantification of how the number and nature of amino acid residues engaged by the ligand influence the docking score, a predictive measure of binding

affinity. Notably, the test compound Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl) exhibits the highest number of amino acid contacts within the α-glucosidase enzyme's active site compared to other ligands, including miglitol and native ligands, correlating with its superior docking score. This outcome underscores the power of computational docking simulations combined with AI-driven visualization to elucidate detailed molecular interactions and predict ligand efficacy with high precision [41].

The results of docking score and amino acids can be used to determine the potential test compounds as antidiabetes mellitus type II, where the smaller the docking score, the greater the number of amino acid bonds formed. Based on the results of this study showed that the compound of Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl), Methyl oleate, Methyl palmitate, Phytol, 9,12,15-Octadecatrien-1-ol, Nerolidol and Eicosane has the smallest docking score value, which is -96.30, -90.59, -87.67, -87.40, -83.27, -81.15, -80.52 among 31 other compounds. Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl), Methyl oleate, Methyl palmitate, Phytol, 9,12,15-Octadecatrien-1-ol, Nerolidol, and Eicosane are the best candidates as antidiabetic mellitus type II to inhibit α-glucosidase enzyme.

Incorporating computational modeling approaches, such as the Ant Colony Optimization algorithm used in this study, significantly enhances the elucidation of drug-target interactions by enabling efficient in silico screening of phytochemicals against diabetic targets. These AI-driven methods accelerate the identification of promising compounds by simulating molecular docking, thus providing detailed insights into binding affinities and interaction stability without the immediate need for costly experimental procedures.

4 Conclusion

This study employed advanced computational techniques, specifically molecular docking powered by ACO algorithm, to screen phytochemicals from *Syzygium polyanthum* for potential antidiabetic drug candidates targeting the α-glucosidase enzyme. The AI-driven molecular docking analysis identified Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl), Methyl oleate, Methyl palmitate, Phytol, 9,12,15-Octadecatrien-1-ol, Nerolidol, and Eicosane as the most promising compounds, exhibiting docking scores of -96.30, -90.59, -87.67, -87.40, -83.27, -81.15, and -80.52, respectively, which indicate stronger and more stable binding affinities compared to the native ligand and the comparator drug miglitol. These results highlight the capability of AI-enhanced molecular docking to efficiently predict and prioritize bioactive compounds with potential therapeutic effects against type II diabetes mellitus, streamlining the drug discovery process by reducing reliance on traditional trial-and-error methods and accelerating the identification of effective α-glucosidase inhibitors.

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