Molecular docking and pharmacokinetic prediction of herbal derivatives as maltase–glucoamylase inhibitor

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MOLECULAR DOCKING AND PHARMACOKINETIC PREDICTION OF HERBAL DERIVATIVES AS MALTASE-GLUCOAMYLASE INHIBITOR

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INTRODUCTION

Diabetes syndrome is a metabolic disorder, which causes congenital (type I insulin-dependent) or acquired (type II noninsulin-dependent) diabetes mellitus, and approximately 7% of the world population is suffering from this chronic disorder [1-4]. This chronic disease not only affects the carbohydrate metabolism but also alters lipid and protein metabolism in advanced stages, leading to complications such as microvascular or macrovascular which are more fatal than the primary diabetic state; thus, all credit goes to regulating postprandial glucose levels [5-7]. One of the therapeutic approaches to regulate blood glucose level in an individual with type 2 diabetes is to inhibit R-amylases and intestinal glucosidases activity using R-glucosidase inhibitors such as acarbose and miglitol [8-10].

Currently, acarbose and miglitol are the only α-glucosidase inhibitors which make up a class of antihyperglycemic drugs for regulating postprandial glucose levels by reversibly inhibiting digestive α-amylases and α-glucosidases [11-14]. Generally, it was believed that carbohydrate mimics contain nitrogen; for instance, acarbose and miglitol are protonated in the active site and act as glucosidase inhibitors due to their ability to mimic the shape or charge of the presumed transition state for enzymatic glycocide hydrolysis [15].

N-terminal catalytic domain of maltase-glucosamylase (ntMGAM) is responsible for the digestion of terminal starch products left after R-amylase action into glucose. This membrane-bound enzyme contains two catalytic subunits: N-terminal subunit (ntMGAM) proximal to the membrane-bound end and C-terminal luminal subunit (ctMGAM) [16,17]. Therefore, to inhibit the enzyme’s function, herbal drugs have been used to replace the synthetic drugs such as acarbose and miglitol which often present adverse effects to some diabetic individuals. Studies showed extracts from Momordica charantia, Tinospora cordifolia, and Zingiber officinale herbal plants to contain alkaloid compounds with α-glucosidase inhibitory properties with hypoglycemic effect on several animal studies and small-scale human studies [18-21]. Moreover, it has been reported that consumption of M. charantia in raw or juice form can be efficacious in lowering blood glucose levels [22,23].

The previous study on molecular docking revealed that momordicoside F2, beta-sitosterol, and cis-N-feruloyltyramine compounds have higher binding affinity to MGAM receptor with the potential to cure type 2 diabetes. However, the structural function and molecular properties for their drug-likeness remain unknown. Related on in silico studies have indicated molecular docking to be a robust and reliable approach to screen for drug-likeness of molecules [24-26]. In drug discovery, structure-based drug design is a vital tool for the discovery and development of new molecules using X-ray crystal structure of a protein from protein data bank (PDB) [27-30]. In molecular modeling, drug-receptor complex stability, exact binding mode, and ligand interaction with amino acids of the protein molecule can be visualized using various docking approaches to discover the pharmacological properties of drug molecules [31].

The current study utilizes in silico molecular docking and pharmacodynamics prediction to elucidate the drug-likeness, Lipinski’s rule, and absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties of momordicoside F2, beta-sitosterol, and cis-N-feruloyltyramine herbal derivatives as MGAM inhibitor.
MATERIALS AND METHODS

Ligands and protein preparation

The three herbal derivatives were selected based on previous network pharmacology study [32]. The 3D ligands structure of beta-sitosterol (CID: 222284) from the Z. officinale herb, cis-N-feruloyltyramine (CID: 5280537, also known as Moupinamide) from Tinospora crispe herb, and momordiciside F2 (CID: 44445567) from M. charantia as well as the standard drug miglitol (CID: 441314) were all downloaded from PubChem online database [33].

The crystal structure of receptor MGAM (PDB code 2QM) protein was downloaded from RCSB PDB [34] at a resolution of 1.9 Å and refined by subtracting water molecules as well as the addition of hydrogen bond and Gasteiger-Huckel charges. All the data files for ligands and receptor were then saved in PDBQT format.

Docking protocol

The AutoDock Vina [35] program installed in 4 GHz Intel Core i3 processor and 4GB RAM, having Windows 8 Professional as an operating system, was utilized to perform automated docking studies to predict the protein–ligand interaction. The active site for MGAM (2QM) was selected and the grid size was set as x = −27.643, y = −12.49, and z = −0.5599 with the box size set to z = 30, y = 30, and x = 36. In addition, the number of exhaustiveness was set at 20 to compromise the global search and local minimum for optimal docking results. To validate the docking protocol for the three herbal derivatives, miglitol was used as the standard ligand. In the proposed docking protocol, ligands were kept flexible while amino acid in protein was held rigid after which each ligand was docked onto the active site of the MGAM receptor [36-38]. The scoring function (Gibbs-free energy/binding affinity) for the ligand–MGAM complex was computed using AutoDock Vina program, while interaction between MGAM amino acids residues and herbal derivatives with respect to H-bond and hydrophobic bonds on the binding sites was analyzed using LigPlot v.1.4 program [39].

The AutoDock Vina program uses free energy empirical scoring functions where binding energy decomposes into several energy components including hydrogen bond, ionic interaction, hydrophobic effect, and binding entropy. AutoDock scoring function is calculated by the equation below:

$$\Delta G = \Delta G_{c} + \Delta G_{rew} + \Delta G_{hb} \times N_{HB} \sum_{\text{neutralH-bond}} f(\Delta R, \Delta a) + \Delta G_{po} \sum_{\text{aromatic}} f(\Delta R, \Delta a) + \Delta G_{p} \sum_{\text{spontaneous}} * f(\Delta R)$$

Where $\Delta G$ is the estimated free binding energy; $\Delta G_{c}$ is the regression constant; $\Delta G_{rew}$, $\Delta G_{hb}$, and $\Delta G_{po}$ are regression coefficients for each corresponding free energy term; $f(\Delta R, \Delta a)$ is scaling function for penalizing ideal geometry deviations; $N_{HB}$ is the number of free rotatable bonds that are immobilized in the complex [40].

Prediction of molecular properties

Lipinski’s rule of five (ROS) was used to evaluate drug-likeness to determine if the herbal derivatives have certain pharmacological or biological activity that would make them an orally active drug-like moiety for humans [41,42]. Thus, essential molecular properties such as molecular weight, hydrogen bond donor, hydrogen bond acceptor, number of the rotatable bonds, and logP for each herbal derivatives (momordiciside F2, cis-N-feruloyltyramine, and beta-sitosterol) were calculated using MedChem Designer (www.simulations-plus.com).

Prediction of bioactivity score

Bioactivity of momordiciside F2, cis-N-feruloyltyramine, and beta-sitosterol herbal derivatives can be checked by calculating the activity score of G-protein-coupled receptor (GPCR) ligand, ion channel modulator, nuclear receptor ligand, kinase inhibitor, protease inhibitor, and enzyme inhibitor [43]. All these parameters were calculated using Molinspiration drug-likeness (www.molinspiration.com), an online server database. Here, calculated drug-likeness scores for each herbal derivative were then compared with that of standard drug miglitol.

Prediction of ADMET properties for the herbal derivatives

Drugs are often withdrawn at the different phases of the clinical trials due to poor ADMET properties and adverse effects probably associated with their molecular structures. Therefore, it is important to predict ADMET properties during the lead identification and optimizations. Here, we used ADMET SAR a free online server to predict ADMET properties such as blood–brain barrier (BBB), penetration, human intestinal absorption (HIA), biodegradability, CaCO2 permeability, AMES toxicity, carcinogenicity, rat acute toxicity. Thus, we estimated the ADMET properties of the compounds using admetSAR online database (www.lmmd.ecust.edu.cn) which comprises data for different entities linked with known ADMET profiles [44].

Therapeutic target validation

Structural feature of a molecule in drug design plays an essential role in correcting therapeutic targets or therapeutic disease. Here, prediction of activity spectra for substances (PASS), an online software tool that predicts more than 300 pharmacological effects and biochemical mechanisms of compounds based on their structural information [45], was used to screen the possible therapeutic targets for the herbal derivatives. PASS (Prediction of activity spectra for substances) software, predicted the probability of activity (Pa) and inactivity (Pi) values for each herbal derivatives to identify the possible inhibitory targets.

RESULTS AND DISCUSSION

In the current study, the binding affinity and binding site similarity (BSS) score for herbal derivatives and standard drug miglitol onto MGAM receptor were evaluated by molecular docking approach using AutoDock Vina software. The molecular properties and biological activity of the herbal derivatives were further analyzed by online tools to predict their pharmacokinetics and pharmacodynamics profiles as future candidate compounds to develop the antidiabetic drug.

The chemical structure and function of momordiciside F2, cis-N-Feruloyltyramine and beta-sitosterol herbal derivatives (Fig. 1) were utilized to predict scoring functions and their biological interaction with amino acid residues of MGAM receptor previously obtained from Protein Data Bank. From the docking analysis binding pattern of herbal derivatives were found to vary with the molecular conformation of the ligand [46-48].

The previous pharmacophore study showed momordiciside F1 and miglitol to have similar BSS score (100%) to MGAM receptor. However, H-bond interactions for both compounds with MGAM were different. Miglitol compound was involved in H-bond interaction with four amino acid residues (Asp702, Leu727, Glu719, Leu725) of MGAM with binding affinity of -5.3 Kcal/Mol whereas, momordiciside F1 interacted with Gln708, Glu704, Try626 and Ile725 amino acid residue with -7.8 Kcal/Mol binding affinity. In addition, the momordiciside F2 compound was also involved in H-bond interaction with seven amino acids of MGAM protein (Lys724, Asp702, Leu727, Glu719, Leu725) and Ile725) of MGAM with binding affinity of -5.3 Kcal/Mol whereas, momordiciside F1 interacted with Gln708, Glu704, Try 626 and Ile725 amino acid residue with -7.8 Kcal/Mol binding affinity. In addition, the momordiciside F2 compound was also involved in H-bond interaction with seven amino acids of MGAM protein (Lys724, Asp702, Leu727, Glu719, Leu725, and Ile725). On the other hand, cis-N-Feruloyltyramine compounds showed a binding pattern with 12 different amino acids residues with six amino acid residues involved in H-bond and hydrophobic interaction at target binding site where four amino acid residues (Glu719, Leu720, Asp702, and Lys724) were involved in the H-bond interaction while two amino acid residues (Ile725 and Glu704) involved in hydrophobic interaction with BSS score (85.71%) and binding affinity (~6.50 Kcal/Mol).

Beta-sitosterol demonstrated high BSS score (85.71%) and binding affinity (~6.8 Kcal/Mol) with MGAM receptor. This explains that its anti-angiogenic potential is due to hydrophobic interactions with MGAM amino acids residues (Ile725, Glu704, Lys724, Glu719, Asp702, and Leu720) with the absence of H-bond interaction. The molecular
docking revealed that the hydrophobic pocket of MGAM comprises nine interaction amino acid residues where four residues (Asp702, Leu727, Ile 725, and Glu719) are responsible for hydrogen bond formation during the interaction while five residues (His728, Gly726, Leu720, Glu704, and Lys 724) form a hydrophobic pocket responsible for direct or indirect hydrophobic interaction. Previous studies have reported that the linker between the polar head and hydrophobic tail plays an important role in binding the ligand with MGAM [49-51]. The previous pharmacophore study revealed three herbal derivatives and standard drug miglitol to have common binding sites (Ile725, Glu704, Lys724, Leu720, Asp702, and Glu719) at MGAM binding pockets. Thus, the binding property of the herbal derivatives onto MGAM indicates their potential to inhibit MGAM activity.

To further understand the molecular properties of the herbal derivatives, we utilize Molinspiration an online tool to analyze the molecular lipophilicity potential (MLP). MLP is a useful property to rationalize various molecular ADMET properties such as membrane penetration or plasma protein binding. Thus, it is important to identify which parts of their molecular surface of a compound are hydrophobic (encoded by violet and blue colors) and/or hydrophilic (encoded by orange and red). MLP analysis (Fig. 2) reveals momordicoside F2, beta-sitosterol, and cis-N-feruloyltyramine to have significant hydrophobicity distribution (83.33%, 100%, and 66.57%, respectively) whereas miglitol showed hydrophilic distribution (57.14%). Hydrophobicity distribution on the molecular surface of the drug molecules plays an important role when distinguishing the observed ADMET properties of drug molecules with respect to their lipophilicity (logP) values [52-54]. The three investigated herbal derivatives show better MLP hydrophobicity distribution as compared to miglitol drug. Therefore, we utilized the calculated MLP from atomic hydrophobicity to compute the logP (Table 1).

The molecular descriptors of herbal derivatives and standard drug miglitol were evaluated for Lipinski’s RO5. From the analysis, cis-N-feruloyltyramine, beta-sitosterol, and miglitol compounds have molecular weight within the range of 200-500 g/Mol, except for momordicoside F2 (618.852 g/Mol) which exceeds the Lipinski’s limit. Molecular weight plays an important role with respect to drug action because as the molecular weight increases beyond the certain limit, the surface area of the compound also increases correspondingly; consequently, this affects the penetrability of the drug compound [55,56]. Likewise, cis-N-feruloyltyramine, beta-sitosterol, and miglitol had similar range for molecular volume, except momordicoside F2 which exceeded the range (603.90). Molecular volume of drug molecule determines its transport characteristics such as intestinal absorption or BBB penetration; hence, it is an important parameter when evaluating molecular properties and biological activity of the investigated herbal derivatives.
Table 1: Docking results and predicted Lipinski’s rule of five for herbal derivatives

| Molecules                          | Lipinski properties | Hydrogen bonding residues | Hydrogen bonding energy (Kcal/Mol) | Hydrogen acceptor | Molecular volume (Å³) | Molecular weight (g/Mol) | LogP | TPSA (Å²) |
|-----------------------------------|---------------------|---------------------------|-----------------------------------|-------------------|-----------------------|--------------------------|------|-----------|
| Miglitol                          |                     |                           |                                    |                   |                       |                          |      | 104.38    |
| cis-N-Feruloyltyramine            |                     |                           |                                    |                   |                       |                          |      | −2.19     |
| Momordicoside F2                  |                     |                           |                                    |                   |                       |                          |      | 100       |
| Beta-sitosterol                   |                     |                           |                                    |                   |                       |                          |      | 4.23      |
| Ile725, Glu704                    |                     |                           |                                    |                   |                       |                          | 618.852 | 78.79     |
| Glu719, Leu727                    |                     |                           |                                    |                   |                       |                          | 313.353 | 76.79     |
| Asp702, Glu719                    |                     |                           |                                    |                   |                       |                          | 289.44  | −2.79     |
| Leu727, Ile725, Glu719            |                     |                           |                                    |                   |                       |                          | 207.226 | 78.79     |

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Prediction of transport properties for herbal derivatives was critical to determine their correlation with the HIA, CaCO₂ monolayers permeability, and BBB penetration. As mentioned previously in the analysis of MLP, lipophilicity (logP) and topological polar surface area (TPSA) play two major factors which influence the permeability of the compounds as well as determine oral bioavailability [57]. The TPSA was obtained by calculating the total surface areas occupied by oxygen and nitrogen atoms as well as hydrogen attached to these molecules. This revealed the relationship of the potential of hydrogen bonding with the TPSA value of those compounds. The lipophilicity for the herbal compound and standard drug miglitol was analyzed by Molinspiration online tool and was found to be logP < 10. In addition, it has been reported that compounds having TPSA ≤ 140 Å and rotational bonds N₀ ≤ 10 are more likely to have good bioavailability due to rotational bonds that make the compounds flexible, hence easily interact with specific rigid binding area [58]. The results indicated that all herbal derivatives and standard drug miglitol demonstrated good numbers of rotational bonds and TPSA value within limits (Table 1).

Drug solubility alongside permeability plays a vital role since those parameters often influence the pharmacokinetic and pharmacodynamics properties of drugs starting from the site of administration, absorption into systemic circulation, and movement in the blood and excretion. Therefore, ADME of the compounds was calculated using online dataset admetSAR mention previously in the materials and methods section. In this analysis, different permeability such as BBB penetration, HIA, CaCO₂ cell permeability, renal organic cation transport, and AMES toxicity were tested. A study has shown that cytochrome P450 (CYP) enzymes are mainly involved in the drug metabolism for elimination and biotransformation. Furthermore, it has been reported that drug–drug interactions can activate or inhibit CYP enzymes; thus, coadministration of the drug may accumulate to toxic level due to inhibition of CYP enzymes or rapid excretion due to activation of CYP microbial enzymes [59]. In clinical pharmacology, P-glycoproteins are the main reason for drug resistance (low cell susceptible to drugs). These proteins are often involved in the efflux and their activation would lead to increase in drug efflux, hence lowering drug concentration below the minimum required level which may result in therapeutic failure [60].

The three investigated herbal derivatives did not show interaction with P-glycoprotein (Table 2). Apart from P-glycoproteins, tumorigenic or carcinogenic may also have a direct or indirect correlation with the molecular properties of those compounds. Thus, carcinogenicity, oral toxicity, and acute dose toxicity in the rat (LD₅₀) of the three compounds were also tested and the results summarized in supplementary file S2. Based on the admetSAR results, all the herbal derivatives can permit through the intestine barrier and absorbed from the human intestine without any toxicity or mutagenicity.

Most drugs often act by interacting with different GPCR ligands, nuclear receptors, or different kind of enzymes, ion channels, protease, viz. kinase. Interaction of chemical compounds with these biomolecules tends to indicate their drug-likeness.

Thus, all the herbal derivatives were screened for their drug-likeness using Molinspiration online tool previously mentioned in the Materials and Methods section (comprehensive results are provided in supplementary file S1). In the analysis, it was hypothesized that molecules having a positive biological value (more than 0.00) are supposed to have good biological activity and those having biological score ≤0.50 are considered to be biologically inactive while compounds with value in between −0.50 and 0.00 are recognized as a mild to moderate active [61]. All the compounds were docked different onto MGAM receptor (a brush border membrane enzyme responsible for digestion dietary starch to glucose) with assumption that the herbal derivatives possess good MGAM inhibitory activity. The predicted biological score (Table 3) indicate that all compounds were biologically

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active with a good biological score <0.00, thus capable of having pharmacological action through interaction with the enzyme receptor.

Although miglitol compound indicated the poor biological score for nuclear receptors (−0.82), a study has reported miglitol drug to have significant biological activity with MGAM in streptozotocin-induced diabetic rats [62]. Both momordicoside F2 and beta-sitosterol herbal derivatives showed a good biological score for kinase inhibition, which may modulate disease state by an alteration in the signal cascading pathway. Furthermore, we performed in silico validation using PASS online software to check the common therapeutic activities for the three investigated herbal derivatives and summarized results in supplementary file S3. The results revealed the herbal derivatives were mainly involved in R-glucosidase, mannosidase, and GPCR kinase 2 (GRK2) inhibitory activities (Table 4). This indicates that momordicoside F2, cis-N-feruloyltyramine, and beta-sitosterol herbal derivative may act as R-glucosidase inhibitor by competitively and reversibly inhibiting alpha-glucosidase in the intestines. Thus, this inhibition lowers the rate of glucose absorption through delayed carbohydrate digestion and extended digestion time [63,64,65]. Hence, the three herbal derivatives may have the probably cure diabetic disease by inhibiting MGAM activity. In addition, momordicoside F2, cis-N-feruloyltyramine, and beta-sitosterol herbal derivatives act as a GRK2 inhibitor. GRK2 can act as an inhibitor of insulin-mediated glucose transport stimulation in 3T3L1 adipocytes by interacting with Gaq/11 function independently of its kinase activity [65]. GRK2 also inhibits basal and insulin-stimulated glycogen synthesis in mouse liver FL83B cells [66]. In that context, PASS validation results revealed that the investigated herbal derivatives have higher probability of inhibiting GRK2 activity and this may play a relevant physiological role in the modulation of insulin responses [67,68]. Studies have shown GRK2 expression is increased in key tissues in different experimental models of insulin resistance, and a 50% downregulation of GRK2 levels in hemizygous GRK2−/− mice is sufficient to protect against TNF-α, aging, or high-fat diet-induced alterations in glucose homeostasis and insulin signaling, strongly arguing for a key role for GRK2 in the modulation of insulin sensitivity in physiological and pathological conditions [69,70]. From this analysis, momordicoside F2, cis-N-feruloyltyramine, and beta-sitosterol herbal derivatives show a significant therapeutic activity with glucosidasas and GRK2; thus, the herbal derivatives may be promising lead compounds for the development of other MGAM inhibitors.

**CONCLUSION**

Discovery of new alpha-glucosidase (MGAM) inhibitors with potential biological activity and minimal or no adverse effect is an exigent need for efficient treatment of diabetes. The current study successfully utilizes molecular docking and pharmacokinetic predictions of momordicoside F2, cis-N-feruloyltyramine, and beta-sitosterol herbal derivatives as MGAM inhibitor in the treatment of diabetes disease. Docking results revealed the three investigated herbal derivatives significantly interaction with MGAM amino acid residues in respect to their inhibitory activities.

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**Table 2: Predicted ADMET properties for herbal derivatives and standard drug miglitol**

| Molecules       | Human intestinal absorption | CaCO-2 permeability | P-glycoprotein substrate | Renal organic transporter | CYP450 3A4 inhibitor | CYP450 2D6 inhibitor | CYP inhibitory promiscuity | HERG inhibition |
|-----------------|----------------------------|---------------------|--------------------------|--------------------------|-----------------------|-----------------------|--------------------------|------------------|
| Miglitol        | 0.5422                     | 0.7375              | 0.6354                   | 0.6749                   | 0.9931                | 0.9535                | 0.9969                   | 0.5797           |
| cis-N-Feruloyltyramine | 0.9884                   | 0.5778              | 0.6064                   | 0.7233                   | 0.6972                | 0.7674                | 0.6502†                  | 0.9668           |
| Monomordicoside F2 | 0.6325                   | 0.8532              | 0.6589                   | 0.7706                   | 0.9600                | 0.9453                | 0.9105†                  | 0.9556           |
| Beta-sitosterol  | 1.0000                     | 0.7953              | 0.6877                   | 0.8098                   | 0.8309                | 0.9364                | 0.5244†                  | 0.8027           |
|                 | HIA+                       | CaCO₂               | Substrate                | Non-inhibitor            | Non-inhibitor         | Non-inhibitor         | Low CYP inhibitory promiscuity | Weak inhibitors |

ADMET: Absorption, distribution, metabolism, excretion, and toxicity, CYP: Cytochrome P450, HIA: Human intestinal absorption, †Significant value

**Table 3: Predicted biological interaction for herbal derivatives and standard drug miglitol**

| Molecules       | GPCR ligand | Ion channel modulator | Kinase inhibitor | Nuclear receptor ligand | Protease inhibitor | Enzyme inhibitor | P-glycoprotein substrate | CYP450 1A2 inhibitor | CYP450 2C9 inhibitor |
|-----------------|-------------|-----------------------|-----------------|-------------------------|-------------------|-----------------|--------------------------|----------------------|---------------------|
| Miglitol        | −0.41       | −0.10                 | −0.53           | −0.82                   | 0.11              | 0.36            | 0.7325                   | 0.927                | 0.9022               |
| cis-N-Feruloyltyramine | 0.10        | −0.06                 | −0.16           | 0.05                    | −0.05            | 0.02            | 0.7851                   | 0.7056               | 0.6571               |
| Monomordicoside F2 | 0.26        | −0.39                 | 0.48            | 0.23                    | 0.20              | 0.30            | 0.6589                   | 0.8953               | 0.8537               |
| Beta-sitosterol  | 0.14        | 0.04                  | 0.51            | 0.73                    | 0.07              | 0.51            | 0.681                    | 0.9291               | 0.9125               |
|                 |             |                       |                 |                         | Non inhibitor     | Non inhibitor   | Non inhibitor             | Non inhibitor        |                     |

GPCR: G-protein-coupled receptor; CYP: Cytochrome P450

**Table 4: Common therapeutic activities for momordicoside F2, cis-N-feruloyltyramine, and beta-sitosterol herbal derivatives**

| Therapeutic activity          | Probability of activity (Pa) | Probability of inactivity (Pi) |
|------------------------------|------------------------------|--------------------------------|
| Mannosidase inhibitor        | 0.963                        | 0.000                          |
| Alpha-mannosidase inhibitor  | 0.960                        | 0.000                          |
| Mannosyl-oligosaccharide 1,2-alpha-mannosidase inhibitor | 0.897 | 0.001 |
| Oligo-1,6-glucosidase inhibitor | 0.893 | 0.001 |
| Sucrose alpha-glucosidase inhibitor | 0.880 | 0.000 |
| Alpha-glucosidase inhibitor  | 0.879*                       | 0.001                          |
| Glucan 1,4-beta-glucosidase inhibitor | 0.517 | 0.006 |
| G-protein-coupled receptor kinase 2 inhibitor | 0.550* | 0.025 |
| Glucose-6-phosphate translocase inhibitor | 0.542* | 0.006 |

*Significant inhibitory activities
to H-bonding and hydrophobic interaction. The similarity score and binding affinity support the hypothesis that three herbal derivatives from Z. officinale, T. crispa, and M. charantia medicinal plants may have substantial antidiabetic property by inhibiting MGAM activity. Moreover, pharmacodynamics prediction of a biological score and ADMET activity indicates the three herbal derivatives could be promising lead molecules for the development of the novel antidiabetic agents, and in the future analogs, compounds hold immense potential to develop a competent therapy for diabetes. However, further in vitro and in-vivo studies will help decipher potential biological activity of the three herbal derivatives with MGAM as an alpha-glucosidase inhibitor with significant antidiabetic effects.

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