INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

In Silico Analysis of Active Compounds in Brotowali *(Tinospora crispa)* as Antihyperglycemic Agents against α-Amylase Receptors

Ishrolana Lutfi Anggraeni[1*], Caca Engellina[2], Imelda Eka Fitriananda[3], Wan Faizah Faradibah Andarista[4], Mohammad Rofik Usman[5]

[1.]Student of Pharmacy, Faculty of Health Sciences, Universitas dr. Soebandi, 68111
[2.]Student of Pharmacy, Faculty of Health Sciences, Universitas dr. Soebandi, 68111
[3.]Student of Pharmacy, Faculty of Health Sciences, Universitas dr. Soebandi, 68111
[4.]Student of Pharmacy, Faculty of Health Sciences, Universitas dr. Soebandi, 68111
[5.]Bachelor of Pharmacy, Faculty of Health Sciences, Universitas dr. Soebandi, 68111
Email: lanalutfi56@gmail.com

Submitted: 27 Juli 2025 Accepted: 30 Juli 2025 Published: 31 Juli 2025

ABSTRACT

Hyperglycemia is a condition characterized by higher than normal blood sugar levels and is the main sign of diabetes mellitus. According to the International Diabetes Federation (IDF) in 2021, Indonesia ranks fifth with 19.47 million diabetics and a population of 179.72 million, and this makes the prevalence of diabetes in Indonesia 10.6%. One of the plants that is widely used as traditional medicine to reduce blood sugar levels is the brotowali plant *(Tinospora crispa)*. This study aims to analyze the mechanism of active compounds of the brotowali plant (Tinospora crispa) that can inhibit the α-amylase enzyme through molecular tethering in silico. This study uses the method of tethering to receptors obtained from the PDB database (ID 1OSE). The positive control used was acarbose so as to obtain a new antihyperglycemic drug candidate with a good pharmacokinetic profile. The molecular tethering simulation results showed that the DL-Carnitine compound has the lowest ΔG value of -4.32 kcal/mol with a Ki value of 680.33 μM and a hydrophobic bond that plays an active role with the natural ligand ASP A:197. In terms of pharmacokinetics, the DL-carnitine compound is better than acarbose. It can be concluded that the DL-Carnitine compound is predicted to be carried out further as research as an antihyperglycemic candidate through α-amylase inhibition.

Key words: *α-Amylase, brotowali, antihyperglycemic, molecular tethering*

INTRODUCTION

Hyperglycemia is a condition characterized by blood sugar levels that are higher than normal and is the main sign of diabetes mellitus. This condition can be caused by various factors, including insulin resistance, pancreatic beta cell dysfunction, or a combination of both (Fardi & Firmansyah, 2024). Risk factors that play a role in this include obesity, lack of physical activity, a diet rich in carbohydrates and fats, and heredity. If not treated properly, long-term hyperglycemia can cause serious problems such as heart and blood vessel disease, kidney damage, visual impairment, and nerve

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

damage (Magliano & Boyko, 2021). In 2021, the International Diabetes Federation (IDF) noted that Indonesia was ranked fifth with 19.47 million people with diabetes and a population of 179.72 million. This makes the prevalence of diabetes in Indonesia 10.6% (Rilwanu, Taufikurachman, Faris Huwaidi, Perangkat Lunak, & Daerah Cibiru, 2022).

One approach to treating hyperglycemia is to inhibit the carbohydrate-digesting enzyme, namely the α-amylase enzyme (Klara, Purwono, & Achmadi, 2023). The α-amylase enzyme is one of the enzymes that functions in the process of catalyzing the 1,4 glycosidic bond in starch and converting it into glucose that can be absorbed by the body; if glucose in the blood exceeds the normal limit, it is stated that diabetes mellitus occurs (Alfiani, 2022). In the treatment of diabetes mellitus, a pharmacological therapy that can be used is the synthetic drug acarbose. Acarbose is a type of synthetic drug that can inhibit the action of the α-amylase enzyme (Diana Nurrah, Tiara Ajeng, & Danang, 2024). The side effects of long-term use of acarbose can cause bloating, diarrhea, and abdominal pain (Hidayah, Pratama, & Raharjo, 2023). This states that there are still many weaknesses in synthetic treatments that encourage people to seek alternative treatments using traditional medicine.

The use of traditional medicine is still popular among the Indonesian people because it is considered efficacious and relatively cheaper and very rarely has side effects (Adiyasa & Meiyanti, 2021). Therefore, the use of traditional medicine is often used by the community as an alternative treatment compared to the use of synthetic drugs. One of the medicinal plants that is empirically used to treat hyperglycemic diseases and for which there have been scientific research reports to prove its efficacy is the brotowali plant *(Tinospora crispa)* (Elfahmi, Santoso, & Anggardiredja, 2019).

The brotowali plant is a plant that is already known as a medicine; this plant climbs upwards and is a plant that likes hot places. The stem of this plant is the size of a little finger (Hasan, Djuwarno, Hiola, Ramadhani, & Halada, 2024). The brotowali plant *(Tinospora crispa)* is one of the family medicinal plants that is effective as an antihyperglycemic (Fatikhurokhmah & Agustini, 2022). The content of chemical compounds that are efficacious as medicine is found in all parts of the plant, from the roots and stems to the leaves. In general, the brotowali plant contains various chemical compounds, including soft resin, starch, glycosides, picroretosid, harsa, the bitter substance picroretin, tinocrisposide, berberine, palmatin, columbine, caoculin or picrotoxin, terpenoids, flavonoids, and alkaloids (Fatikhurokhmah & Agustini, 2022). Therefore, the development of effective drugs for the treatment of hyperglycemia is very important.

According to Widodo, Santjojo, Widyarti, and Sumitro (2021), the brotowali plant has 6 active compounds confirmed by LCMS analysis, including betaine, DL-carnitine, ferulic acid, adenosine, choline, and berberine. However, computational research on these active compounds to see the interaction between ligands and catalytic residues of α-amylase has never been carried out. This study aims to analyze the mechanism of active compounds of brotowali *(Tinospora crispa)* that can inhibit the α-amylase enzyme through in silico molecular docking.

Scientific proof of medicinal plants or herbs needs to be done, one of which is by utilizing computer technology. One method used is an in silico study. In silico studies are carried out to increase the efficiency of the drug design process by utilizing computers.

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

In silico studies involve a database with relevant molecular structures that are then docked to the target protein (Klara et al., 2023). It is hoped that this study will find active ingredients of brotowali that can function as inhibitors of α-amylase receptors in the treatment of hyperglycemia.

MATERIAL AND METHODS

Tools

This research uses a laptop tool, the ACER One Z1402, with specifications of Windows 10 Home Single Language 64-bit, Intel® Celeron® 2957U @1.40GHz (2 CPUs). The applications used for docking are AutoDockTools version 1.5.6 and PyRx v0.9.8. The applications used for preparation and visualization are MarvinSketch v24.1.0, Molegro Molecular Viewer v2012.2.5, and Discovery Studio Visualizer v24.1.0.

Materials

The materials used in this study are the ligand file and the α-amylase enzyme (PDB code: 1OSE) in PDB (.pdb) and PDBQT (.pdbqt) formats. The natural ligand used is beta-D-glucopyranose with the positive control ligand acarbose and six chemical compounds from the plant brotowali, including betaine, DL-carnitine, ferulic acid, adenosine, choline, and berberine, as test ligands obtained from the research by Widodo et al. (2021).

Prediction of Pharmacokinetic Profile

The pharmacokinetic prediction of ligands was performed on all test ligands and positive controls. The overall structure of the ligands was downloaded from the PubChem website in SMILES format. The prediction of ligand bioactivity was carried out using Lipinski's Rule of Five. This prediction was performed using online software SCFBio (Klara et al., 2023).

Preparation of Ligands and Receptors

The structures of betaine, DL-carnitine, and choline were downloaded from the PubChem site in .pdb format, then pasted into MarvinSketch software, structured in 2D, and saved. The structure of the protein α-amylase (PDB ID: 1OSE) was downloaded from the RCSB Protein Data Bank. The receptor was downloaded from the Protein Data Bank in .pdb format (PDB ID: 1OSE)

Validation of Molecular Docking Method

This method is validated by re-docking the natural ligand to the active site of the protein with a repetition of 100 times, producing grid box output and RMSD (Root Mean Square Deviation) value parameters. RMSD is measured in Å (Ångström) (Ruswanto, Mardianingrum, & Yanuar, 2022). Molecular docking parameters are considered valid if the RMSD value is < 2.0 Å (Sari, Junaidin, & Pratiwi, 2020).

Molecular Docking

Molecular docking is performed using the AutoDockTools 1.5.6 program. The grid box coordinates are determined based on the co-crystal coordinates from the receptor file used during validation. The molecular docking process is carried out according to the parameters in the molecular docking method validation. Molecular docking is performed using the Command Prompt (cmd) (Sari et al., 2020).

Visualization of Receptor-Ligand Interaction

Data analysis was performed using BIOVIA Discovery Studio 2024 by visualizing the 2D structure of the bond between the ligand, which is a compound from brotowali, and the α-amylase receptor (1OSE). Based on the binding energy generated from molecular docking, the binding energy value indicates the strength of the bond between the test compound and the receptor. The lower the binding energy, the stronger the bond between the compound and the receptor (Afriana & Dewi, 2022).

RESULT AND DISCUSSION

In silico testing is conducted as an effort in the discovery of new drugs with the aid of computers. This computational method test is an experiment that illustrates the interaction between a compound or ligand and its target molecule (Chandra et al., 2024). In this test, Lipinski's Rule of Five (RO5) testing was performed on 6 active compounds, namely betaine, DL-carnitine, ferulic acid, adenosine, choline, and berberine in the brotowali plant, as well as on the drug compound acarbose as a positive control.

Prediction of Pharmacokinetic Profile

Test compounds are said to meet the requirements for being formulated as oral preparations if there is no more than one violation of Lipinski's rules (Chandra et al., 2024). These rules have five parameters that must be met, namely molecular weight <500 Da, log P value <5, number of hydrogen bond donors <5, number of hydrogen bond acceptors <10, and molar refractivity values ranging from 40 to 130 (Klara et al., 2023). This can lead to fewer hydrogen molecules being able to pass through the cell membrane. Compounds categorized as drug-like molecules are predicted to be able to penetrate the gastrointestinal membrane and cell membranes and can easily reach target proteins if they meet these rules.

The natural ligands that have been inputted according to Lipinski's Rule of Five show a natural ligand molecular weight of 312.000 g/mol, a log P value of <-0.05, fewer than 5 hydrogen bond donors, fewer than 6 hydrogen bond acceptors, and a molar refractivity value of less than 77.145. According to the journal by Widodo et al. (2021), the brotowali plant contains 6 active compounds confirmed by LCMS analysis, including betaine, DL-carnitine, ferulic acid, adenosine, choline, and berberine. Based on **Table 1**, the active compounds from the brotowali plant *(Tinospora crispa)* that meet and pass Lipinski's Rule of Five (RO5) for natural ligands are only 3 compounds, namely betaine, DL-carnitine, and choline. The prediction results of these 3 active compounds from the brotowali plant were modeled in 2D and 3D, and these 3 active compounds demonstrate that the compounds tested have a good pharmacokinetic profile, allowing them to be tested in the next stage.

Preparation of Ligands and Receptors

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

At this stage, ligand protonation occurs to adjust to a blood pH of around 7.4. Simultaneously, a conformational step is performed to achieve the molecular position at the lowest or most stable energy to enable interaction with the active site of the receptor. The test protein used is α-amylase (PDB ID: 1OSE). This protein complex consists of a receptor with the natural ligand beta-D-glucopyranose. The preparation of this receptor aims to remove water content that could impede the interaction of the ligand with the receptor (Ruswanto et al., 2022).

Validation of Molecular Docking

The visualization of the validation results shows a comparison of the ligand positions before and after docking. The validation results on the α-amylase receptor, as shown in **Figure 5**, display the best position of the natural ligand, as the natural ligand before (yellow) and after (green) docking overlap each other. The molecular docking validation of the α-amylase protein (1OSE) used a grid box size of 46 x 40 x 48 Å (Ångström) and coordinates x, y, and z (37.388, 38.479, and -1.606 Å) against the natural ligand beta-D-glucopyranose. The best validation result was found in run 6 with an RMSD value of 1.45 Å. A molecular docking method is deemed valid if the RMSD (Root Mean Square Deviation) value is < 2 Å (Sari et al., 2020). A smaller RMSD value indicates that the position of the ligand from the repeated molecular docking is getting closer to the position of the ligand from crystallography (Nursamsiar, Mangande, Awaluddin, Nur, & Asnawi, 2020). This validation result means that the size and coordinates of the grid box can be used for docking test compounds.

RMSD (Root Mean Square Deviation) is a deviation value that represents the comparison between the ligand-receptor conformation during the ongoing simulation process and the initial ligand-receptor conformation (Dermawan, Sumirtanurdin, & Dewantisari, 2019). **Figure 6** shows that the RMSD value of the natural ligand interacts stably because it is the natural ligand of the receptor.

Molecular Docking Results

Gibbs free energy/affinity energy (ΔG) is obtained from the results of molecular docking. The value of ΔG is a stability parameter of the conformation between the ligand and receptor and is also a predictor of the spontaneity of a reaction. A negative ΔG value indicates that a reaction occurs spontaneously, while a positive ΔG value indicates that the reaction is non-spontaneous. The value of ΔG is produced when the formed ligand-receptor complex can show the ligand's affinity for its receptor. A low ΔG value indicates a high affinity of the ligand for the receptor; conversely, a high ΔG value indicates a low affinity of the ligand for the receptor. Inhibition constant (Ki) analysis is also performed to determine the inhibitory power of a compound against its receptor. A smaller Ki value indicates a stronger inhibition of the compound. A decreasing ΔG value from molecular docking leads to a smaller Ki value. Both parameters can serve as references in determining the best compound (Kalontong, Safithri, & Tarman, 2022).

The natural ligand beta-D-glucopyranose has a ΔG value of -8.20 kcal/mol with a Ki value of 971.70 nM, and the positive control acarbose has a ΔG value of -4.05 kcal/mol with a Ki value of 1.08 μM. Among all the compounds tested as ligands in this study, only DL-carnitine has a ΔG value lower than that of the positive control acarbose, which is -

4.32 kcal/mol, and a Ki value of 680.33 μM **(Table 2)**. This DL-carnitine compound is interpreted as having conformational stability closer to the natural ligand, better than the positive control and other test ligands. The directly proportional ΔG and Ki values indicate that DL-carnitine has inhibitory activity against α-amylase that is also close to that of the natural ligand.

Visualization of Receptor-Ligand Interaction

The visualization of the molecular docking results was performed to observe the docking outcomes of natural ligands, positive controls, and test ligands against the α-amylase receptor used, as well as to analyze the interactions and types of ligand-receptor bonds. **Figure 7** shows the 2D interaction between the ligands and amino acid residues (protein). Observing the amino acid residues aims to identify the interactions occurring between the ligands and the receptor. The interactions will be more stable and better between the compounds and the amino acid residues if they have hydrogen bonds. The more hydrogen bond interactions between the compounds and the amino acid residues, the more stable and favorable the interaction is predicted to be (Mardianingrum, Bachtiar, Susanti, Nuraisah, & Ruswanto, 2021).

The same amino acid residues in the test ligand and the target receptor indicate that the test compound interacts stably with the receptor binding site and exhibits competitive activity. Based on the amino acid residues obtained from each test ligand in **Figure 7**, it is estimated that DL-Carnitine has a stable binding and also has the lowest ΔG value, which is closest to the natural ligand.

Protein Analysis Test with Ramachandran Plot

The PROCHECK examination using the Ramachandran plot (**Figure 8**) focuses on regions with unusual geometries and allows for an overall assessment of the structure. To determine if the protein structure has a good analysis, the results on the Ramachandran plot can be observed using the plot of non-glycine residues, where the disallowed regions should be less than 0.8% (Ruswanto, Mardianingrum, Nofianti, Fizriani, & Siswandono, 2023).

Based on the Ramachandran plot, the percentage of residues in the favored, allowed, and disallowed regions of the α-Amylase compound complex (1OSE) can be observed in **Figure 8**. From **Figure 8**, it can be seen that the α-Amylase complex (1OSE) has gem-shaped residues in the favored region at about 88.1%, and there are no residues in the disallowed region. In conclusion, the quality of the α-Amylase complex (1OSE) can be said to be stable.

CONCLUSION

Based on the results of the research conducted, out of 6 active compounds of the brotowali plant, which include betaine, DL-carnitine, ferulic acid, adenosine, choline, and berberine, it was found that only 3 compounds meet the physicochemical requirements of Lipinski's Rule of Five. Overall, the brotowali plant has the potential to be developed as an antihyperglycemic drug due to 1 compound that has a better binding affinity than the positive control. The best compound is DL-Carnitine, which has the lowest ΔG value of -4.32 kcal/mol with a Ki value of 680.33 μM and hydrophobic interactions that play an

active role with the natural ligand ASP A:197. Therefore, from a pharmacokinetic perspective, DL-carnitine is better than acarbose. It can be concluded that the compound DL-Carnitine is predicted to be subject to further research as a candidate for antihyperglycemic through the inhibition of α-amylase (1OSE).

ACKNOWLEDGEMENT

With all due respect, the author expresses the utmost gratitude to all parties who have assisted in the process of compiling this journal, especially the supervising lecturer who has provided valuable facilities, support, and motivation in the preparation of this journal. Thanks are also extended to colleagues and all parties who contributed to the smooth running of this activity. It is hoped that this journal can provide positive contributions to the development of science and serve as inspiration for future research.

REFERENCES

Adiyasa, M. R., & Meiyanti, M. (2021). Pemanfaatan Obat Tradisional di Indonesia: Distribusi dan Faktor Demografis yang Berpengaruh. *Jurnal Biomedika Dan Kesehatan, 4*(3), 130-138.

Afriana, D., & Dewi, C. (2022). Studi In Silico Senyawa Dari Saffron *(Crocus sativus L.)* Terhadap Reseptor Glikogen Sintase Kinase-3 Beta (GSK-3β) Sebagai Antidiabetes. *Jurnal Pharmacia Mandala Waluya, 1*(5), 188-201.

Alfiani, L. A. (2022). Uji Aktivitas Penghambatan Enzim α–amilase oleh Ekstrak Herba Ciplukan (*Physalis Angulate L*) Secara In Vitro. *Jurnal Ilmiah Wahana Pendidikan, 8*(15), 335-346.

Chandra, J. H., Azalia, A. S., Lestari, V. W., Khairani, S., Saepudin, A. H., & Hasanah, A. N. (2024). Studi In Silico Aktivitas Senyawa Anti Inflamasi Asam Jawa Sebagai Inhibitor COX-2. *Jurnal Kesehatan Tambusai, 5*(3), 5871-5880.

Dermawan, D., Sumirtanurdin, R., & Dewantisari, D. (2019). Molecular Dynamics Simulation Estrogen Receptor Alpha againts Andrographolide as Anti Breast Cancer. *Indonesian Journal of Pharmaceutical Science and Technology, 6*(2), 65-76.

Diana Nurrah, A., Tiara Ajeng, L., & Danang, R. (2024). Aktivitas Penghambatan Enzim α-Amilase Ekstrak Etanol dan Fraksi Buah Belimbing Wuluh *(Averrhoa bilimbi L.)*. *OBAT: Jurnal Riset Ilmu Farmasi dan Kesehatan, 2*(6), 114-132. doi:10.61132/obat.v2i6.813

Elfahmi, E., Santoso, W., & Anggardiredja, K. (2019). Uji Aktivitas Antidiabetes Produk Obat Herbal yang Mengandung Ekstrak Bratawali *(Tinospora crispa (L.)* Miers ex Hoff. f & Thoms.). *Jurnal Sains Farmasi & Klinis, 6*(3), 213-219.

Fardi, F., & Firmansyah, F. (2024). Bakti Kesehatan: Pemeriksaan Kesehatan & Penyuluhan Kesehatan Tentang Waspada Hipertensi, Hiperglikemia, Hiperurisemia, dan Hiperkolesterolemia. *PEDAMAS (PENGABDIAN KEPADA MASYARAKAT), 2*(05), 1362-1371.

Fatikhurokhmah, H. M., & Agustini, R. (2022). Concentration Effect of Brotowali Stem (*Tinospora Crispa (L.)*) in Ethanol Extracts on the A-Glukosidase Enzyme Inhibition. *Indonesian Journal of Chemical Science, 11*(3), 241-249.

Hasan, H., Djuwarno, E. N., Hiola, F., Ramadhani, F. N., & Halada, I. O. (2024). Penapisan Fitokimia Dan Uji Efek Antidiabetes Ekstrak Metanol Daun Brotowali *(Tinospora crispa L.)* Pada Mencit *(Mus musculus)*. *Journal of Pharmacology and Natural Products (JPNP), 1*(1), 20-31.

Hidayah, N., Pratama, K. J., & Raharjo, D. (2023). Aktivitas Penghambatan Enzim Alfa-amilase Ekstrak Dan Fraksidaun Nipah *(Nypa fruticans Wurmb)*. *Jurnal Ilmiah Wahana Pendidikan, 9*(25), 677-684.

Kalontong, P. K., Safithri, M., & Tarman, K. (2022). Penambatan Molekul Senyawa Aktif Spirulina Platensis Sebagai Inhibitor TMPRSS2 untuk Mencegah Infeksi SARS-COV-2. *Jurnal Pengolahan Hasil Perikanan Indonesia, 25*(2), 253-267.

Klara, I. K., Purwono, R. M., & Achmadi, P. (2023). Analisis In Silico Senyawa Flavonoid Kayu Secang *(Caesalpinia sappan L.)* pada Reseptor α-Amilase sebagai Antihiperglikemik. *Acta VETERINARIA Indonesiana, 11*(3), 210-219.

Magliano, D. J., & Boyko, E. J. (2021). IDF Diabetes Atlas 10th Edition Scientific Committee. *IDF DIABETES ATLAS [Internet]. 10th ed. Brussels: International Diabetes Federation, 35914061*.

Mardianingrum, R., Bachtiar, K. R., Susanti, S., Nuraisah, A. N. A., & Ruswanto, R. (2021). Studi In Silico Senyawa 1, 4-Naphthalenedione-2-Ethyl-3-Hydroxy sebagai Antiinflamasi dan Antikanker Payudara. *ALCHEMY Jurnal Penelitian Kimia, 17*(1), 83-95.

Nursamsiar, N., Mangande, M. M., Awaluddin, A., Nur, S., & Asnawi, A. (2020). In Silico Study of *aglycon curculigoside* A and its Derivatives as α-amilase Inhibitors. *Indonesian Journal of Pharmaceutical Science and Technology, 7*(1), 29-37.

Rilwanu, F., Taufikurachman, H., Faris Huwaidi, D., Perangkat Lunak, R., & Daerah Cibiru, K. (2022). Penerapan Algoritma K-Nearest Neighbor untuk Mendeteksi Diabetes Berbasis Web Application. *Journal of Software Engineering, Information and Communication Technology, 3*(1), 145-152.

Ruswanto, R., Mardianingrum, R., Nofianti, T., Fizriani, R., & Siswandono, S. (2023). Computational Study of Bis-(1-(Benzoyl)-3-Methyl Thiourea) Platinum (II) Complex Derivatives as Anticancer Candidates. *Advances and applications in bioinformatics and chemistry*, 15-36.

Ruswanto, R., Mardianingrum, R., & Yanuar, A. (2022). Computational Studies of Thiourea Derivatives as Anticancer Candidates Through Inhibition of Sirtuin-1 (SIRT1). *Jurnal Kimia Sains dan Aplikasi, 25*(3), 87-96.

Sari, I. W., Junaidin, J., & Pratiwi, D. (2020). Studi Molecular Docking Senyawa Flavonoid Herba Kumis Kucing (*Orthosiphon Stamineus B.)* Pada Reseptor A-Glukosidase Sebagai Antidiabetes Tipe 2. *Jurnal Farmagazine, 7*(2), 54-60.

Widodo, W., Santjojo, D., Widyarti, S., & Sumitro, S. (2021). Exploring and Proving Complex Compounds in Brotowali *(Tinospora crispa)*. *RASAYAN J. Chem, 14*(4), 2666-2670.

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

TABLE AND FIGURE

Table 1. Lipinski's Rule of Five Data

Compound	Molecular Weight (<312.000 g/mol)	Hydrogen Donors (<5)	Hydrogen Acceptors (<6)	Log P (<-0.05)	Molar Refractivity (<77.145)
Betaine	**117.148**	**0**	**2**	**-1.55**	**49.125**
DL-Carnitine	**161.201**	**1**	**3**	**-1.80**	**66.649**
Ferulic Acid	194.186	2	3	1.4986	81.065
Adenosine	267.245	4	9	-1.98	106.846
Choline	**104.173**	**1**	**1**	**-0.31**	**44.963**
Berberine	336.367	0	4	3.0963	144.867

Table 2. The results of molecular docking of acarbose and test compounds from the bitter plant against the α-amylase enzyme.

Compound	Run	ΔG (kkal/mol)	Ki	RMSD (Å)	Amino Acid Interactions	
					Hydrogen Bond	Hydrophobic Bond
Ligan alami (Beta-D-glucopyranose)	6	-8.20	971.70 nM	1.45	HIS A:201, LYS A:200, HIS A:305, GLU A:233, ASP A:300, HIS A:299, GLN A:63, ALA A:107	TYR A:151, GLU A:240, GLY A:306, ILE A:235, HIS A:101, LEU A:162, ASP A:197, ALA A:198, TYR A:62, ARG A:195, TRP A:58, VAL A:163, TRP A:59, GLY A:164, GLY A:106, SER A:105, GLY A:104, LEU A:165
Kontrol positif (Acarbose)	100	-4.05	1.08 µM	49.30	**HIS A:201**, **GLU A:233, ASP A:300,HIS A:305**	-
Betaine	95	-3.50	2.70 µM	53.81	ILE A:235	VAL A:234, **TYR A:151**, HIS A:201, **LEU A:162**, ALA A:198, LYS A:200, GLU A:233
DL-Carnitine	19	-4.32	680.33 µM	52.08	ILE A:235	HIS A:201, **ASP A:197**, GLU A:233, ASP A:300, LYS A:200
Choline	62	-4.14	925.18 µM	52.21	-	HIS A:201, ASP A:300, GLU A:233, LYS A:200

Description: Gibbs Free Energy/Affinity Energy (ΔG); Inhibition Constant (Ki)

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

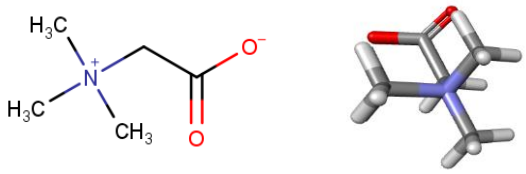


Figure 1. 2D and 3D of Betaine Ligand

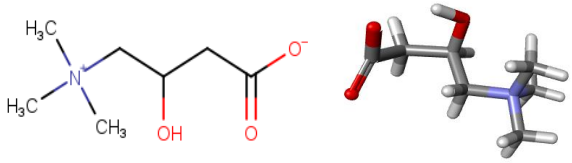
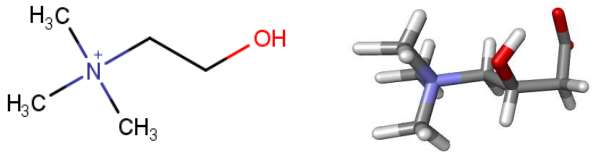


Figure 2. 2D and 3D structure of DL-Carnitine



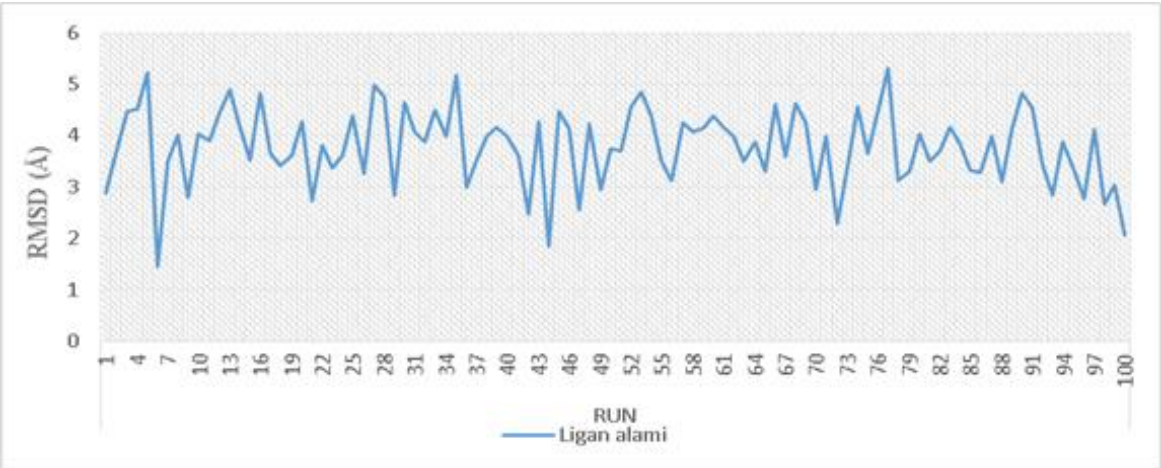


Figure 4. 3D Receptor α-amylase (PDB ID: 1OSE)

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS

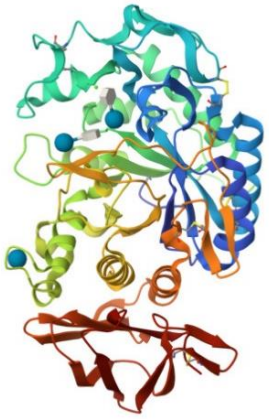
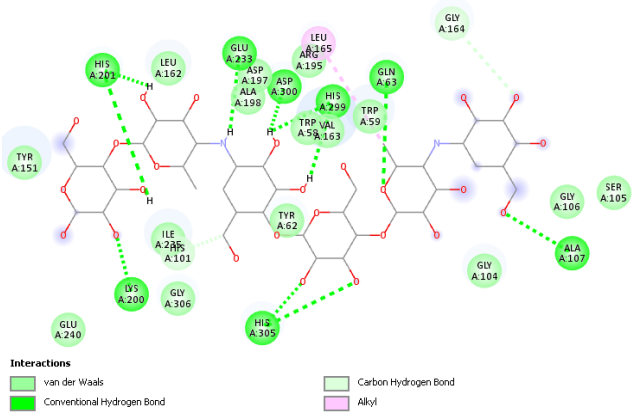
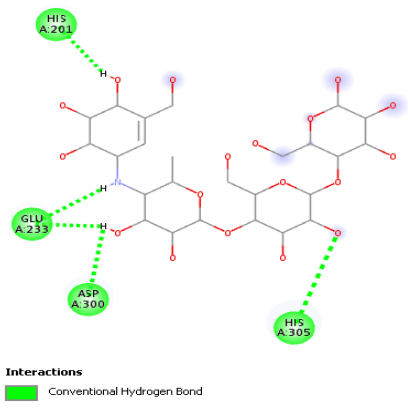


Figure 5. Illustration of the overlap of natural ligands before (yellow) and after (green) anchoring.

Figure 6. RMSD graph of Natural Ligand



a) Natural ligand (Beta-D-glucopyranose)

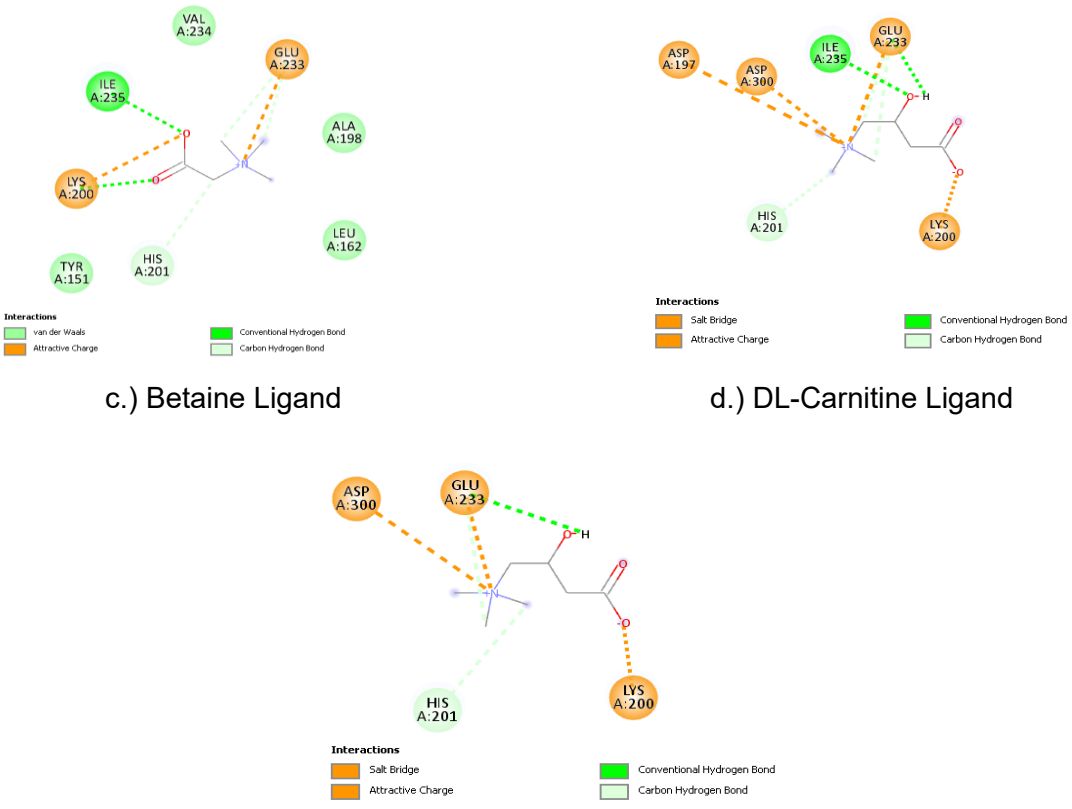


b) Positive control (Acarbose)

INDONESIAN PHARMACOPEIA JOURNAL

IPJ Vol. 2 No. 2, Tahun 2025
Online ISSN : 3032-5455

RESEARCH ARTICLE OPEN ACCESS



c.) Betaine Ligand

d.) DL-Carnitine Ligand

e.) Choline Ligand

Figure 7. 2D Interaction of Receptors with Natural Ligand, Positive Control, and Test Ligand

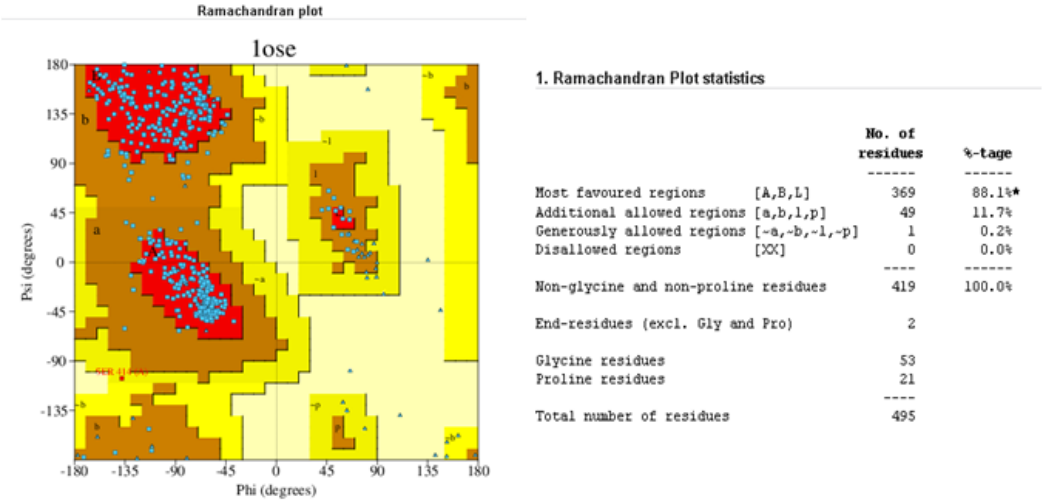


Figure 8. Ramachandran Plot of the α-amylase Protein (1OSE)