**Exploring Acetylcysteine, L-Glutathione and Acetyl-L-Carnitine as α-Glucosidase Inhibitors through Molecular Docking Studies for Diabetes Treatment**

Virgitha Yustanari Kusuma Putri1), Triyanda Gunawan1,a) and Yuly Kusumawati1,b)

Author Affiliations

*1Department of Chemistry, Faculty of Science and Data Analytics, Sepuluh Nopember Institute of Technology,*

*ITS Sukolilo Campus, Surabaya 60111, East Java, Indonesia.*

*a)*Corresponding author*:* [*triyanda@its.ac.id*](mailto:triyanda@its.ac.id)

*b)*[*y\_kusumawati@chem.its.ac.id*](mailto:y_kusumawati@chem.its.ac.id)

**Abstract.** Diabetes is a chronic disease that cannot be cured, resulting in an escalating number of patients annually. Consequently, α-glucosidase inhibition has emerged as a crucial strategy to prevent surges in blood glucose levels. Proteins like Acetylcysteine, L-Glutathione, and Acetyl-L-Carnitine are anticipated to function as α-glucosidase inhibitors. Traditionally, Acetylcysteine has been utilized as a mucolytic medication in Indonesia, while L-Glutathione and Acetyl-L-Carnitine have been employed as multivitamin supplements. In this study, molecular docking simulations were conducted between the 8EMR protein and Acetylcysteine, L-Glutathione, and Acetyl-L-Carnitine using the Autodock Vina program, with binding free energy and inhibition constant (Ki) as the parameters. The findings revealed that Acetylcysteine, L-Glutathione, and Acetyl-L-Carnitine possess the capability to inhibit α-glucosidase, exhibiting binding free energies of -3.69, -2.46, and -4.41 kcal/mol, respectively, and inhibition constants (Ki) of 1.96 mM, 15.78 mM, and 583.54 μM. This research concluded that Acetylcysteine, L-Glutathione, and Acetyl-L-Carnitine can effectively inhibit α-glucosidase and serve as potential alternatives to reduce blood glucose levels.

**Keywords**: *Diabetes, Antidiabetic Agent, Acetylcysteine, L-Glutathione, Acetyl-L-Carnitine, α-glucosidase, AutodockTools, SDG.*

# INTRODUCTION

Diabetes mellitus, a chronic metabolic condition characterized by elevated blood glucose levels, affects millions of people worldwide. One of the main methods used to treat diabetes is controlling blood glucose levels by blocking enzymes that are involved in carbohydrate metabolism [1–3] . According to figures from the International Diabetes Federation (IDF), Indonesia is in the top 5 countries with the greatest prevalence of diabetes [4]. This is a problem that we must address, particularly because this figure will increase over time. The explanation of this expansion is that individuals with diabetes cannot be cured; they can only achieve remission and reduction until the condition no longer recurs [5]. Diabetes is a genetic condition that is influenced by both one's eating habits and family history [6]. In Indonesia, people are accustomed to and have a strong dependence on fast food and sugary meals, leading to a steady rise in the number of individuals affected by diabetes each year. There are two types of diabetes. Individuals with Type 1 diabetes are characterized by their inability to produce sufficient amounts of insulin or a complete lack of insulin production. The treatment for this patient involves administering insulin by injection. In type 2 diabetes, there is impairment to both the receptor and the production of insulin. Therefore, managing type 2 diabetes is a difficult task that cannot be only accomplished by the administration of insulin injections [5]. Currently, a ketogenic diet is employed to decrease blood glucose levels [6]. The a-glucosidase protein in human blood breaks down carbohydrates and other sources into glucose. By inhibiting a-glucosidase, one aims to induce remission of diabetes. Alpha-glucosidase inhibitors prevent the absorption of carbohydrates in the small intestine. They compete to inhibit the enzymes responsible for converting indigestible complex carbohydrates into easily absorbable simple carbohydrates [7–16]. In recent years, there has been growing interest in natural compounds as potential α-glucosidase inhibitors and acetylcysteine, L-glutathione, and acetyl-L-carnitine have emerged as promising candidates. The distinctive structural and functional properties of these compounds may contribute to their ability to block α-glucosidase [17].

The antioxidant and mucolytic properties of acetylcysteine, a derivative of a semi-essential amino acid, have been extensively studied [7, 18]. Acetylcysteine is readily accessible in Indonesian pharmacies as a cough medicine. Acetylcysteine is a promising candidate for further investigation as a potential antidiabetic medication due to recent findings suggesting its potential α-glucosidase inhibitory activity. L-glutathione, a tripeptide composed of glutamic acid, cysteine, and glycine, is a potent antioxidant found in virtually all living cells. The neuroprotective and cognitive-enhancing properties of acetyl-L-carnitine, an ester derivative of the amino acid L-carnitine, have been extensively studied. Recent investigations have defined its potential as an α-glucosidase inhibitor, indicating that it might be used in the treatment of diabetes and other metabolic illnesses [19].

For the new diabetes treatments, particularly in light of recent statistics highlighting Indonesia's high diabetes prevalence, we will employ cutting-edge molecular docking techniques. This computational approach, which represents the latest trend in drug discovery, will be used to predict the binding interactions between these compounds and the 8EMR protein [20, 21]. By conducting simulations to analyze the affinities and binding patterns of acetylcysteine, L-glutathione, and acetyl-L-carnitine with the 8EMR protein, scientists can get a deeper understanding of how these substances hinder the protein's activity. This knowledge can help identify promising compounds for further exploration. This study aims to assess the inhibitory ability of acetylcysteine, L-glutathione, and acetyl-L-carnitine as α-glucosidase inhibitors. Molecular docking studies will be conducted against the 8EMR protein to explore their effectiveness. Our research focuses on understanding the molecular interactions and binding characteristics involved in order to develop more effective therapeutic strategies for treating diabetes and related metabolic disorders.

Our main focus is on computational elements of α-glucosidase inhibitor investigations. We restrict the scope of our study to in silico simulations and analysis, especially molecular docking methods. This computational method enables us to easily and cost-effectively anticipate and evaluate molecular interactions between the examined drugs (acetylcysteine, L-glutathione, and acetyl-L-carnitine) and the target 8EMR protein. While these computational tools are effective in providing preliminary insights into possible inhibitors, it should be noted that these in silico results require additional confirmation by in vitro and in vivo experimental trials. This constraint enables us to focus on the predictive and mechanistic elements of drug-target interactions, laying a solid foundation for future experimental study. We hope that our targeted and comprehensive approach will have a significant influence on the early stages of diabetic drug development. However, we realize the need for more study to confirm our computational findings in more complex biological systems.

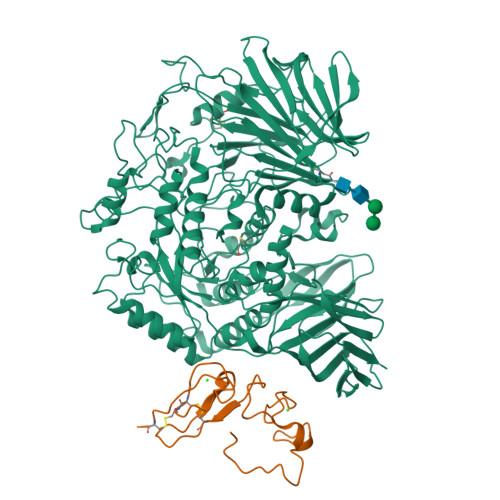
# METHODS

The crystal structure of α-glucosidase protein (PDB ID: 8EMR) was obtained from the Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data Bank [22]. Using AutoDockTools 1.5.6 package the protein file was inserted and prepared, including removing hetero atoms and water molecules from the protein structure, as well as adding polar hydrogen and Kollman charges. In order to prepare the protein for futur e ligand binding, the mineral ligand was extracted from the structure [23, 24]. Moreover, the protein is composed of three chains A, B, and C. The chemical structures of Acetylcysteine, L-glutathione, and acetyl-L-carnitine were acquired from the PubChem database [25–27]. The obtained structures were subsequently converted into forms compatible with Open Babel 3.1.1 from sdf to pdbqt [28, 29]. The ligands were individually docked into the binding site of α-glucosidase (PDB ID: 8EMR) using Lamarckian genetic algorithm with autodock 4. The conformations with the highest scores were subsequently determined based on their projected binding affinities. The docking findings were examined and presented using PyMOL version 3.0, as well as using Protein-Ligand Interaction Profiler (PLIP), Proteinsplus poseview and LigPlot+ [30–36]. The main objective was to identify possible hydrophobic, hydrogen bonding, and other significant interactions between the ligands and the residues in the active site.

# RESULT AND DISCUSSION

Molecular docking techniques have been used to investigate the level of atomic interactions between small molecules and receptors. This approach provides valuable insight into the behavior of small molecules in the attachment sites of protein targets [37]. It also helps to explain biological processes, particularly the binding of amino acids to the active site. By observing these molecular interactions, researchers can gain further understanding of the mechanisms underlying drug-receptor interactions and protein function. Molecular docking can be used to observe the interactions between the α-glucosidase protein (PDB ID: 8EMR) and ligands Acetylcysteine, L-glutathione, and acetyl-L-carnitine. The α-glucosidase protein (PDB ID: 8EMR) was chosen due to its effectiveness in remission of type 2 diabetes [38]. This docking research on 8EMR, an α-glucosidase in the human liver is expected to aid in diabetes treatment, especially type 2, in humans before clinical trials are conducted [22, 39–41]. Acetylcysteine, L-glutathione, and acetyl-L-carnitine are amino acids that are commonly regarded as antioxidants. Acetylcysteine, L-glutathione, and acetyl-L-carnitine have many active sites that can inhibit the 8EMR protein (**Fig 1**).

The antioxidant and mucolytic properties of acetylcysteine, a derivative of a semi-essential amino acid, have been extensively studied. Acetylcysteine is readily accessible in Indonesian pharmacies as a cough medicine, whilst L-glutathione and acetyl-L-carnitine are used as antioxidants or cosmetic products. The Lipinski's rule of five parameters apply to acetylcysteine, L-glutathione, and acetyl-L-carnitine. Acetylcysteine, having a molecular weight of 163.2 g/mol, a logP value of 0.4, 3 hydrogen bond donors, 4 hydrogen bond acceptors, and 3 rotatable bonds, complies with all of Lipinski's requirements. L-glutathione has a molecular weight of 307.33 g/mol, which is within the permitted range. The compound's logP value of -4.5 shows a strong affinity for water, and it possesses 6 hydrogen bond donors, which exceeds the acceptable amount. Acetyl-L-carnitine, which has a molecular weight of 203.24 g/mol and a logP value of 0.4, meets the requirements for both molecular weight and lipophilicity. The molecule possesses 3 hydrogen bond donors, 4 hydrogen bond acceptors, and 9 rotatable bonds. According to Lipinski's principles, the study shows that acetylcysteine and acetyl-L-carnitine possess advantageous drug-like characteristics. However, L-glutathione may have difficulties in being absorbed by the body when taken orally since it has a greater number of hydrogen bond donors and is very hydrophilic. These findings offer valuable information on the possible pharmaceutical uses of these compounds, namely in terms of their drug-like properties and potential for being taken orally (**TABLE 1**) [25–27]. Acetylcysteine, L-glutathione, and acetyl-L-carnitine are probable α-glucosidase inhibitors, according to docking data in the dlg file.





**Figure 1.** The structure of (a) 8EMR, (b) acetylcysteine, (c) L-glutathione, (d) acetyl-L-carnitine

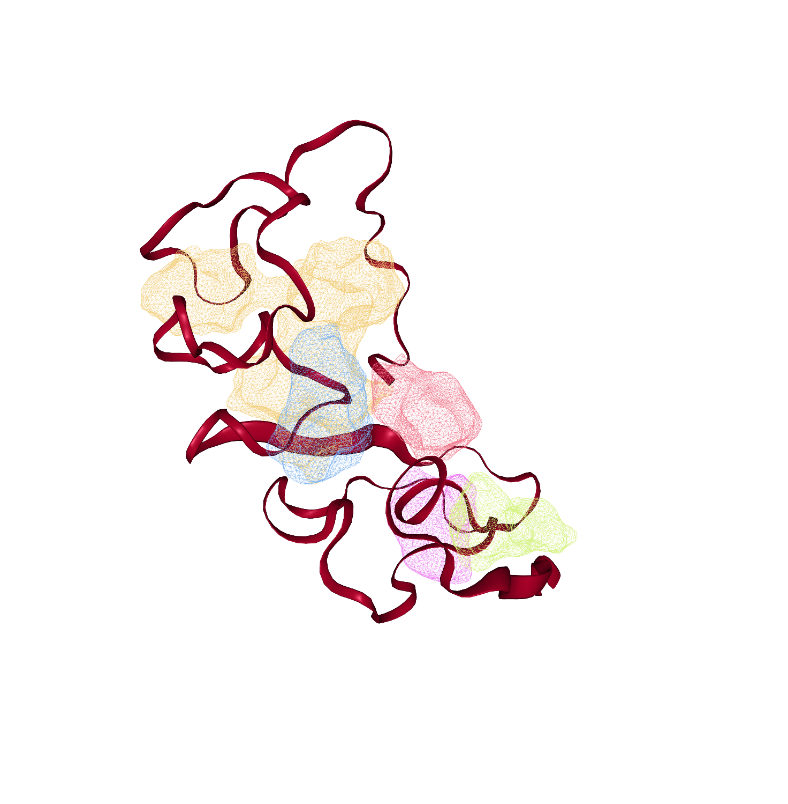
## TABLE 1. The Lipinski rule of five for acetylcysteine, L-glutathione and acetyl-L-carnitine.

| **Ligand** | **Molecular Weight (<500 Da)**  **(g/mol)** | **logP**  **(<5)** | **H-Bond Donor (<5)** | **H-Bond Acceptor (<10)** | **Rotatable Bond (5)** |
| --- | --- | --- | --- | --- | --- |
| Acetylcysteine | 163.2 | 0.4 | 3 | 4 | 3 |
| L-glutathione | 307.33 | -4.5 | 6 | 8 | 9 |
| acetyl-L-carnitine | 203.24 | 0.4 | 0 | 4 | 5 |

**TABLE 2** shows the results of protein binding pocket/site prediction for 8EMR, providing crucial details on the likely places where this protein may interact with drugs. The table displays five distinct binding locations, each delineated by distinctive features. Binding site 1 has the highest volume (788.43 Å³), surface area (1242.24 Å²), drug score (0.81), and simple score (0.56). Based on the data, site 1 is the most favorable option for pharmacological interactions, the subsequent binding sites (2-5) shows a steady reduction in both volume and surface area, with site 5 being the smallest in size (with a volume of 100.86 Å³ and a surface area of 227.05 Å²). It is worth mentioning that sites 2, 3, and 4 consistently have drug scores between 0.23 and 0.25. However, their simple scores differed, with sites 3 and 4 having a value of zero. Site 5, although being modest, has a drug score of 0.18. An extensive analysis of the characteristics of the binding site yields useful insights for the development and refinement of medications that specifically target the 8EMR protein. This might potentially result in the creation of more potent pharmaceutical drugs[42]. The color-coding in the table corresponds to visual representations in **Fig 2**, offering a complementary view of these binding sites.

## TABLE 2. The Lipinski rule of five for acetylcysteine, L-glutathione and acetyl-L-carnitine.

| **Binding site** | **Colour** | **Volume (A3)** | **Surface (A2)** | **Drug Score** | **Simple Score** |
| --- | --- | --- | --- | --- | --- |
| 1 |  | 788.43 | 1242.24 | 0.81 | 0.56 |
| 2 |  | 163.97 | 311.47 | 0.25 | 0.03 |
| 3 |  | 140.54 | 333.44 | 0.23 | 0 |
| 4 |  | 120.51 | 385.08 | 0.23 | 0 |
| 5 |  | 100.86 | 227.05 | 0.18 | 0 |



**Figure 2.** Binding pocket/site prediction of 8EMR

The docking results indicate that acetylcysteine, L-glutathione, and acetyl-L-carnitine can interact with the 8EMR protein. GLU105B interacts hydrophobically with the active site of acetylcysteine, while CYS112B interacts with it via a hydrogen bond (**Fig 3a**). There is a hydrophobic connection between PRO71B and the L-glutathione active site, as well as hydrogen bond interactions between GLY2A, GLY2A, CYS70B, CYS70B, PRO71B, and ASN90B and the L-glutathione active site (**Fig 3b**). Acetyl-L-carnitine has hydrophobic contacts with PHE75B, hydrogen bond interactions with LEU25B, THR78B, THR103B, and the active site of acetyl-L-carnitine, and π-cation interactions with TYR106B (**Fig 3c**). **TABLE 3** shows how acetylcysteine, L-glutathione, and acetyl-L-carnitine interact with the 8EMR protein. The Root Mean Square Deviation (RMSD) of the docking clusters was found to be 0 Å, falling below the 1.2 Å criterion. This result is highly significant in molecular docking studies. An RMSD of 0 Å shows complete alignment between the predicted ligand posture and the reference structure. Values below 1.2 Å are typically recognized as indicative of extremely excellent alignment. These low RMSD values indicate a high level of trust in the docking simulations' correctness and the predictability of protein-ligand interactions [43].



**Figure 3.** The interactions of 8EMR with (a) acetylcysteine, (b) L-glutathione, (c) acetyl-L-carnitine

## TABLE 3. The interactions of 8EMR with acetylcysteine, L-glutathione, and acetyl-L-carnitine.

| **Ligand** | **cluster RMSD** | **Number of Interaction** | |  | | **Amino acid Involved in Interaction** | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **H-Bond** | **Hydrophobic** | | **π-Cation Interactions** | | **H-Bond** | **Hydrophobic** | **π-Cation Interactions** | |
| Acetylcysteine | 0 | 1 | 1 | | - | | CYS112B | GLU105B | - | |
| L-glutathione | 0 | 6 | 1 | | - | | GLY2A, GLY2A, CYS70B, CYS70B, PRO71B, ASN90B | PRO71B | - | |
| acetyl-L-carnitine | 0 | 4 | 1 | | 1 | | LEU25B, THR78B, THR78B, THR103B | PHE75B | TYR106B | |

Metformin, a typical medicine, has a binding energy of -5.40 kcal/mol with the active site of α-glucosidase, according to previous investigations [44–47]. The binding affinity of the α-glucosidase 8EMR protein with acetylcysteine, L-glutathione, and acetyl-L-carnitine is -3.69, -2.46, and -4.41 kcal/mol (**TABLE 4**). These findings suggest that the ligands acetylcysteine, L-glutathione, and acetyl-L-carnitine have the potential to acquire binding affinities similar to metformin. Acetylcysteine, L-glutathione, and acetyl-L-carnitine create a stable complex with the target protein to inhibiting α-glucosidase 8EMR. In this molecular docking investigation, the estimated inhibitory constant (Ki) values for interactions between the 8EMR protein and acetylcysteine, L-glutathione, and acetyl-L-carnitine were 1.96 mM, 15.78 mM, and 583.54 μM. The inhibition constant value is half the maximal inhibition of an enzyme by a chemical substance and is used to measure a substrate/inhibitor's ability to enhance or inhibit protein biology and function. Potential inhibitors are defined as those with a lower inhibition constant (Ki) [48].

Comparative insights are crucial for assessing their effectiveness as α-glucosidase inhibitors. Intermolecular Energy refers to the interaction energy between the ligand and the protein, lower values signify a higher binding affinity. Internal Energy indicates the stress within the ligand molecule during binding, negative values imply that the ligand retains a stable conformation upon binding. Torsional energy measures ligand flexibility, higher torsional energy may suggest improved adaptation of the ligand to the binding site. Acetylcysteine exhibits balanced properties, characterized by significant intermolecular energy (–5.19 kcal/mol) and moderate torsional energy (1.49 kcal/mol), suggesting stable binding with a degree of flexibility. L-glutathione demonstrates significant stability, with an intermolecular energy of –6.58 kcal/mol, the lowest recorded. However, it may show flexibility because to a higher torsional energy of 3.88 kcal/mol. Acetyl-L-carnitine has an intermolecular energy of -5.49 kcal/mol and a torsional energy of 1.79 kcal/mol, highlight adaptability and effectiveness in binding interactions.

## TABLE 4. The characteristic of 8EMR with acetylcysteine, L-glutathione and acetyl-L-carnitine.

| **Ligand** | **Cluster RMSD** | **Inhibition constant (KI)** | **Intermolecular Energy (kcal/mol)** | **Internal Energy (kcal/mol)** | **Torsional energy (kcal/mol)** | **Binding Energy (kcal/mol)** |
| --- | --- | --- | --- | --- | --- | --- |
| Acetylcysteine | 0 | 1.96 mM | -5.19 | -1.58 | 1.49 | -3.69 |
| L-glutathione | 0 | 15.78 mM | -5.53 | -6.58 | 3.88 | -2.46 |
| acetyl-L-carnitine | 0 | 583.54 μM | -5.49 | -1.08 | 1.79 | -4.41 |

**TABLE 5** shows that Acetylcysteine, L-Glutathione, and Acetyl-L-Carnitine exhibited moderate to strong binding energies (-5.19, -2.46, and -4.41 kcal/mol, respectively), indicating a good potential for stable inhibitor-enzyme complexes that could serve as Metformin alternatives. The Annona muricata study produced promising results, indicating that 15-acetyl guanacone has a high binding affinity (−7.00 kcal/mol) for glucosidase that is better than Metformin (−5.40 kcal/mol) [49]. This shows that plant extracts may be excellent inhibitors of glucosidase and could be helpful in developing new obesity and diabetes treatments. The same could be said for the flavonoids and other natural polyphenols studied, because they also seem to be good inhibitors of glucosidase. Binding energies for both Quercetin and Acarbose hovered around -4.8 to -5.0 kcal/mol, indicating comparable effectiveness to our reference medications, and perhaps even greater reliability due to potential side effects. Furthermore, these flavonoids highlight their potential for regulating postprandial glycemia, offering an effective and safer approach in managing blood sugar level [50]. In summary, all three studies demonstrate significant potential in α-glucosidase inhibition, with plant-based and amino acid-based inhibitors offering viable and natural alternatives to conventional drugs like Metformin and Acarbose. These findings pave the way for further research into natural compounds to improve diabetes treatment strategies.

## TABLE 5. Comparison of α-Glucosidase Inhibition Potency.

| **Ligand** | **Binding Energy (kcal/mol)** | **Inhibitor Type** | **Key Advantages** | **Ref** |
| --- | --- | --- | --- | --- |
| Acetylcysteine | -3.69 | amino acid based | Moderate to strong binding, stable complexes | this paper |
| L-glutathione | -2.46 | amino acid based | this paper |
| acetyl-L-carnitine | -4.41 | amino acid based | this paper |
| Metformin | -5.40 |  |  | [49] |
| 15-acetyl guanacone | -7.00 | plant extract based | Higher binding affinity | [49] |
| Quercetin | -4.80 | polyphenol based | Fewer side effects | [50] |
| Kaempferol | - | polyphenol based | Fewer side effects | [50] |
| Acarbose | ~-5 | polyphenol based | - | [50] |

# CONCLUSION

This study investigates the impacts of Acetylcysteine, L-glutathione, and acetyl-L-carnitine for inhibitions the α-glucosidase protein 8EMR, by evaluating their ability to bind to the established drug metformin. Our molecular docking study, which was validated by RMSD values of 0 Å, categorizes these compounds as very promising inhibitors of 8EMR α-glucosidase. This is owing to their exceptional ligand efficiency and appealing interaction features. This finding is also reinforced by the presence of negative binding energies and low inhibition constants (Ki). Although the computational results are fascinating, they emphasize the significance of thorough experimental validation and optimization. Future research should focus on determining the inhibitory effects using cellular models, confirming the characteristics of protein-ligand interactions, and exploring structural modifications to enhance effectiveness and safety. These discoveries might potentially result in the creation of novel α-glucosidase inhibitors and therapeutic approaches for the treatment of type 2 diabetes. Nevertheless, it is crucial to highlight that more in vitro and in vivo investigations are necessary to fully comprehend the potential of these medicines as safe and effective inhibitors for clinical use.

# ACKNOWLEDGEMENT

The Author gratefully acknowledge financial support from the Institut Teknologi Sepuluh Nopember for this work, under project scheme of the Publication Writing and IPR Incentive Program (PPHKI) 2025.

# REFERENCES

[1] L. F. Schütz, M. H. Park, and M. Choudhury, HDACs in Diabetes, in Nutritional and Therapeutic Interventions for Diabetes and Metabolic Syndrome, Elsevier (2018), pp. 475–486.

[2] R. Makkar, T. Behl, and S. Arora, Current Research in Translational Medicine 68, 45 (2020).

[3] D. P. Christensen, M. Dahllöf, M. Lundh, D. N. Rasmussen, M. D. Nielsen, N. Billestrup, L. G. Grunnet, and T. Mandrup-Poulsen, Mol Med 17, 378 (2011).

[4] D. Magliano and E. J. Boyko, IDF diabetes atlas, Brussels, International Diabetes Federation (2021).

[5] J. M. Forbes and M. E. Cooper, Physiological Reviews 93, 137 (2013).

[6] Z. Bahadoran, P. Mirmiran, and F. Azizi, J Diabetes Metab Disord 12, 43 (2013).

[7] K. C. Agu, N. Eluehike, R. O. Ofeimun, D. Abile, G. Ideho, M. O. Ogedengbe, P. O. Onose, and O. O. Elekofehinti, Clin Phytosci 5, 21 (2019).

[8] M. Genovese, I. Nesi, A. Caselli, and P. Paoli, Molecules 26, 4818 (2021).

[9] J. Hu, X. Lai, X. Wu, H. Wang, N. Weng, J. Lu, M. Lyu, and S. Wang, Foods 12, 183 (2023).

[10] C. Proença, M. Freitas, D. Ribeiro, E. F. T. Oliveira, J. L. C. Sousa, S. M. Tomé, M. J. Ramos, A. M. S. Silva, P. A. Fernandes, and E. Fernandes, Journal of Enzyme Inhibition and Medicinal Chemistry 32, 1216 (2017).

[11] J. Riyaphan, D.-C. Pham, M. K. Leong, and C.-F. Weng, Biomolecules 11, 1877 (2021).

[12] Z. Yin, W. Zhang, F. Feng, Y. Zhang, and W. Kang, Food Science and Human Wellness 3, 136 (2014).

[13] Y. Zhang, F. Zhou, M. Bai, Y. Liu, L. Zhang, Q. Zhu, Y. Bi, G. Ning, L. Zhou, and X. Wang, Cell Death Dis 10, 66 (2019).

[14] H. Zheng, J. Wu, Z. Jin, and L.-J. Yan, Biochem Insights 9, BCI.S36141 (2016).

[15] H. Tateiwa, T. Kawano, A. Nishigaki, D. Yamanaka, B. Aoyama, M. Shigematsu-Locatelli, S. Eguchi, F. M. Locatelli, and M. Yokoyama, Life Sciences 197, 56 (2018).

[16] Y. Xiong, P. Peng, S.-J. Chen, M. Chang, Q. Wang, S.-N. Yin, and D.-F. Ren, Food Chemistry: Molecular Sciences 5, 100139 (2022).

[17] C. Berraquero-García, F. Rivero-Pino, J. L. Ospina, R. Pérez-Gálvez, F. J. Espejo-Carpio, A. Guadix, P. J. García-Moreno, and E. M. Guadix, Food Bioscience 55, 102954 (2023).

[18] R. J. Perry, J.-P. G. Camporez, R. Kursawe, P. M. Titchenell, D. Zhang, C. J. Perry, M. J. Jurczak, A. Abudukadier, M. S. Han, X.-M. Zhang, H.-B. Ruan, X. Yang, S. Caprio, S. M. Kaech, H. S. Sul, M. J. Birnbaum, R. J. Davis, G. W. Cline, K. F. Petersen, and G. I. Shulman, Cell 160, 745 (2015).

[19] S. Lowitt, J. I. Malone, A. Salem, W. M. Kozak, and Z. Orfalian, 42 (1993).

[20] X. Che, Q. Liu, and L. Zhang, Results in Engineering 19, 101335 (2023).

[21] O. L. Erukainure, K. P. Otukile, K. R. Harejane, V. F. Salau, A. Aljoundi, C. I. Chukwuma, and M. G. Matsabisa, Arabian Journal of Chemistry 16, 104842 (2023).

[22] C.-C. Su, M. Lyu, Z. Zhang, M. Miyagi, W. Huang, D. J. Taylor, and E. W. Yu, Cell Reports 42, 112609 (2023).

[23] R. Huey, G. M. Morris, A. J. Olson, and D. S. Goodsell, Journal of Computational Chemistry 28, 1145 (2007).

[24] G. M. Morris, D. S. Goodsell, R. S. Halliday, R. Huey, W. E. Hart, R. K. Belew, and A. J. Olson, J. Comput. Chem. 19, 1639 (1998).

[25] National Center for Biotechnology Information (2024), PubChem Compound Summary for CID 12035, Acetylcysteine, (2024).at <https://pubchem.ncbi.nlm.nih.gov/compound/Acetylcysteine.>

[26] National Center for Biotechnology Information (2024), PubChem Compound Summary for CID 124886, Glutathione, (2024).at <https://pubchem.ncbi.nlm.nih.gov/compound/Glutathione>

[27] National Center for Biotechnology Information (2024), PubChem Compound Summary for CID 7045767, Acetyl-L-Carnitine, (2024).at <https://pubchem.ncbi.nlm.nih.gov/compound/Acetyl-L-Carnitine>

[28] N. M. O’Boyle, M. Banck, C. A. James, C. Morley, T. Vandermeersch, and G. R. Hutchison, J Cheminform 3, 33 (2011).

[29] The Open Babel Package, version 3.1.1at <http://openbabel.org>

[30] The PyMOL Molecular Graphics System, Version 3.0 Schrödinger, LLC.at <https://pymol.org/support.html>

[31] M. F. Adasme, K. L. Linnemann, S. N. Bolz, F. Kaiser, S. Salentin, V. J. Haupt, and M. Schroeder, Nucleic Acids Research 49, W530 (2021).

[32] R. A. Laskowski and M. B. Swindells, J. Chem. Inf. Model. 51, 2778 (2011).

[33] R. Fährrolfes, S. Bietz, F. Flachsenberg, A. Meyder, E. Nittinger, T. Otto, A. Volkamer, and M. Rarey, Nucleic Acids Research 45, W337 (2017).

[34] K. Schöning-Stierand, K. Diedrich, R. Fährrolfes, F. Flachsenberg, A. Meyder, E. Nittinger, R. Steinegger, and M. Rarey, Nucleic Acids Research 48, W48 (2020).

[35] K. Stierand and M. Rarey, ACS Med. Chem. Lett. 1, 540 (2010).

[36] K. Schöning-Stierand, K. Diedrich, C. Ehrt, F. Flachsenberg, J. Graef, J. Sieg, P. Penner, M. Poppinga, A. Ungethüm, and M. Rarey, Nucleic Acids Research 50, W611 (2022).

[37] N. Kerru, A. Singh-Pillay, P. Awolade, and P. Singh, European Journal of Medicinal Chemistry 152, 436 (2018).

[38] H. K. Thabet, A. Ragab, M. Imran, M. Hamdy Helal, S. Ibrahim Alaqel, A. Alshehri, A. Ash Mohd, S. S. Alshammari, Y. A. Ammar, and M. S. Abusaif, RSC Adv. 14, 15691 (2024).

[39] L. S. Jefferson, W. S. Liao, D. E. Peavy, T. B. Miller, M. C. Appel, and J. M. Taylor, Journal of Biological Chemistry 258, 1369 (1983).

[40] F. Oyakhire, E. M.A, E. Ogie, and E. E. Valentine, Med.Lab.Tech.J. 7, 155 (2021).

[41] J. Zhang, O. Pivovarova-Ramich, S. Kabisch, M. Markova, S. Hornemann, S. Sucher, S. Rohn, J. Machann, and A. F. H. Pfeiffer, Front. Nutr. 9, 808346 (2022).

[42] A. Volkamer, D. Kuhn, T. Grombacher, F. Rippmann, and M. Rarey, J. Chem. Inf. Model. 52, 360 (2012).

[43] I. Kufareva and R. Abagyan, Methods of Protein Structure Comparison, in Homology Modeling, Edited by A. J. W. Orry and R. Abagyan, Totowa, NJ, Humana Press (2011), pp. 231–257.

[44] G. Ashraf, D. DasGupta, M. Alam, S. Baeesa, B. Alghamdi, F. Anwar, T. Alqurashi, S. Sharaf, W. Al Abdulmonem, M. Alyousef, F. Alhumaydhi, and A. Shamsi, Molecules 27, 4652 (2022).

[45] R. W. Hunter, C. C. Hughey, L. Lantier, E. I. Sundelin, M. Peggie, E. Zeqiraj, F. Sicheri, N. Jessen, D. H. Wasserman, and K. Sakamoto, Nat Med 24, 1395 (2018).

[46] S. A. Ashraf, A. E. O. Elkhalifa, A. J. Siddiqui, M. Patel, A. M. Awadelkareem, M. Snoussi, M. S. Ashraf, M. Adnan, and S. Hadi, Molecules 25, 2735 (2020).

[47] S. A. Ashraf, A. E. O. Elkhalifa, K. Mehmood, M. Adnan, M. A. Khan, N. E. Eltoum, A. Krishnan, and M. S. Baig, Molecules 26, 5957 (2021).

[48] S. C, D. K. S., V. Ragunathan, P. Tiwari, S. A., and B. D. P, Journal of Biomolecular Structure and Dynamics 40, 585 (2022).

[49] K. C. Agu, N. Eluehike, R. O. Ofeimun, D. Abile, G. Ideho, M. O. Ogedengbe, P. O. Onose, and O. O. Elekofehinti, Clin Phytosci 5, 21 (2019).

[50] E. Barber, M. J. Houghton, and G. Williamson, Foods 10, 1939 (2021).