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Simulation of Interaction Energy of Hemoglobin Docking with Nano Biomaterials for Hypoglycemic Treatment

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Abstract

Simulation of the electronic and thermodynamic properties of deoxyhemoglobin docking with nano Cinnamon and Glucose, as well as the docking of glucose with hypoglycemic medications, were studied using the Gaussian 09 program. The optimized structures of the dockings were executed. The effect of the drug (Forxiga) and (nano Cinnamon) docking with deoxyhemoglobin was ascertained. The results show that the deoxyhemoglobin docking with nano Cinnamon causes a non-spontaneous change in Gibbs free energy. Moreover, the change in enthalpy indicates that every reaction is endothermic. Thus, it can be concluded that, whereas nano Cinnamon ~~is~~ docking with deoxyhemoglobin safe and harmless. Glucose has a negative effect on the human body's circulation. Structures have been modeled and prepared in the GaussView 6.0.16 program using density functional theory at the level (B3LYP), with basis set (6 -311G(d,p)).

Keyword: forxiga • docking, blood sugar • simulation • glucose • nano cinnamon • diabetes.

Introduction

A major metabolic disease called diabetes is characterized by hyperglycemia. Hyperglycemia is a hallmark of diabetes, a metabolic condition that has the potential to be lethal[1]. Compared to the costly and frequently associated with pharmacological techniques of treating diabetes, the use of medicinal herbs is less expensive and has no adverse side effects. Alkaloids, tannins, flavonoids, and other active phytochemicals with medicinal significance are among the many compounds found in medicinal plants. Diabetes can be treated with these phytochemicals[2]. The physiologically active medication used to treat diabetes that is present in nano Cinnamon is covered in this article. It is necessary to consume macronutrients to maintain energy balance. Since it is clear that certain components of macronutrients regulate insulin sensitivity and glucose homeostasis, determining the optimal dietary composition is essential to preventing insulin resistance and type 2[3]. Investigated the mechanisms underlying the impact of various macronutrient components on insulin sensitivity. Numerous studies demonstrate that by using multi-omics analysis (the term “omics” refers to a number of areas of study in biology, all of which end in the suffix -omics, indicating totality of some kind.

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Omics are novel, comprehensive approaches for the analysis of complete genetic or molecular profiles of humans and other organisms. Precision nutrition may be applied more effectively in real-world settings, and the molecular pathways underlying type 2 diabetes can be found, providing a deeper understanding of the relationship between diet and genetics[4]. Studies suggest that there might be a connection between an elevated risk of adverse cardiovascular events and some anti-diabetic medications. Administration of rosiglitazone was found to dramatically increase the risk of myocardial infarction and mortality from cardiovascular causes, in contrast to antidiabetic treatments. This finding was observed in many investigations [5].

To explain how the best medication is found, materials science and a variety of technological applications, such as solar cells, ablation of materials, superconductors, and several docking processes that connect a number of carefully selected drugs commonly used to treat blood sugar with the hormone that causes the disease (blood sugar) can be used. Many times, the best nanomaterial to increase the drug's efficacy in removing blood sugar was chosen[6-9]. Hemoglobin (HB) is a vital protein found in erythrocytes and has the chemical formula $C_{42}H_{45}FeN_7O_5$. It is responsible for carrying oxygen to different parts of the body[10]. Hemoglobin concentrations must be kept at suitable levels in order to guarantee optimal tissue oxygenation. Hemoglobin is a transporter during respiration, making it easier for carbon dioxide to return to the atmosphere and a pathway for oxygen from the pulmonary system to the body's tissues.

People have been using nano Cinnamon for millennia in traditional herbal medicine and as a spice in food[11]. Studies using in vitro and animal models have demonstrated that nano Cinnamon in nanoclusters may have anti-inflammatory, antibacterial, antioxidant, anti-cancer, cardiovascular, cholesterol-lowering, and immunomodulatory properties[12]. Furthermore, strong hypoglycemia effects have been shown in studies involving animals. However, the limited number of well-controlled clinical studies limits the conclusions that can

be made about the potential health benefits of nano Cinnamon for those living in the open.

The inaugural pharmacological agent belonging to a novel category of Glucose co-transporter inhibitors for the oral management of type 2 diabetes is Forxiga[13]. Forxiga (Dapagliflozin) significantly reduces both body weight and HbA1c levels, while concurrently enhancing blood pressure parameters. A hemoglobin A1C (HbA1c) test is a blood test that shows what your average blood sugar (Glucose) level was over the past two to three months. Glucose is a type of sugar in your blood that comes from the foods you eat. Dapagliflozin exhibited a comparable reduction in HBA1c levels relative to sulfonylureas, which are the most frequently prescribed oral antidiabetic agents aside from Metformin; however, it was associated with a greater degree of weight reduction and a notably diminished incidence of hypoglycemic events[14]. Consequently, for patients diagnosed with T2DM who do not achieve adequate glycemic control on Metformin supplemented with dietary modifications and physical activity, dapagliflozin presents a viable alternative to sulfonylureas. For patients with inadequately controlled type 2 diabetes, Forxiga (dapagliflozin) serves as a pioneering oral inhibitor that may be administered as a monotherapy or in conjunction with dietary interventions and exercise to effectively manage the condition[15].

Glucose, an aldose monosaccharide, is an essential metabolic substrate and energy source for a wide variety of organisms. It is involved in both photosynthesis and respiration. Moreover, glucose is an important component of modern food products, especially when it comes to flavor and texture. It also serves as a monomeric unit and a building block for more complex molecular structures like different sugars and glucosides[16]. Numerous cutting-edge techniques have been developed to measure and detect glucose concentrations quantitatively throughout time[17]. However, higher glucose concentrations are associated with higher blood sugar levels, which may eventually hasten the onset of diabetes. The study aims to build up the simulation of the electronic and thermodynamic properties of deoxyhemoglobin docking with nano Cinnamon and Glucose, as well as the docking of glucose with hypoglycemic medications using the Gaussian 09 program.

Theoretical Considerations

The most efficient and secure medication for the treatment of diabetes can be selected by researching the thermodynamic, electronic, and optical characteristics of the medications used to treat the condition by modeling all potential drug interactions between hemoglobin (HB) and blood sugar-lowering medications. Density functional theory (DFT) is a popular computational method for resolving quantum mechanical issues in atoms, molecules, solid state, chemistry, biology, and even nuclear physics. Dispersion adjustments are crucial in many density functional computations involving biomolecules, just as they are in our study[18-20].

There are two different kinds of electronic bands: conduction and valence bands. The outermost area of an atom's or molecule's orbitals and electronic configuration is called the valence. This is the area where external electrons are most likely to be encountered. They are often referred to as HOMOs, or highest-occupied molecular orbitals. There are electrons in this band that are connected to the nucleus. Moreover, the higher energy level, or conduction band, is clearly distinguished from the valence band. It stands for an orbital, or area, in which excited electrons in the valence band can travel. For the electron-free conduction band, the standard is the lowest unoccupied molecular orbital (LUMO). The two most important molecular orbitals are HOMO and LUMO. The difference between LUMO and HOMO energy is called the forbidden energy gap or simply band gap[21]:

$$E_g = (\varepsilon_{LUMO} - \varepsilon_{HOMO}) \quad \text{... (1)}$$

The amount of energy required to release an electron from the system at the ground state reference geometry is called the ionization potential (IP)[22]:

$$IP = -\varepsilon_{HOMO} \quad \text{... (2)}$$

Electron affinity (EA) is known as the amount of energy released when an electron is related to the system[23]:

$$EA = -\varepsilon_{LUMO} \quad \text{... (3)}$$

The Fermi level was defined as the energy of the highest occupied molecular orbital (HOMO) in the valence band at 0 K. Nevertheless, some studies have utilized the mid gap level, calculated from the HOMO and LUMO, as the Fermi energy[24, 25]:

$$E_F = -(IP + EA)/2 \quad \text{... (4)}$$

Work function was symbolized to the minimum energy desired to take out an electron from the Fermi level, and it's computed as the energy variance between the vacuum level (LUMO) and the Fermi level (chemical potential)[26]:

$$\Phi_m = LUMO - E_F \quad \text{... (5)}$$

Electronegativity means compute of the inclination of a system to pull a bonding two of electrons. Electronegativity describes the escape inclination of the electrons from the equilibrium system[22]:

$$\chi = (IP + EA)/2 \quad \text{... (6)}$$

Electrophilicity index measures the stabilization in energy when the system acquires an additional electronic charge from the environment[22, 27]:

$$\omega = \chi^2/2\eta \quad \text{... (7)}$$

The chemical hardness is a measure of the impedance to transporting charge. Chemical hardness can be computed immediately from the equation[22]:

$$\eta = (IP - EA)/2 \quad \text{... (8)}$$

The global chemical softness, ζ, can be defined as a property of molecules that measures the range of chemical reactivity. It is the inverse of the chemical hardness η [22]:

$$\zeta = 1/2\eta \quad \text{... (9)}$$

Any pharmacological drug containing deoxyhemoglobin (DHB) can be docked via four different kinds of binding forces according to thermodynamic properties and the nature of binding forces. Van der Waals forces, hydrogen bonds, hydrophobic interactions, and electrostatic interactions are all

included in these categories. The thermodynamic properties can be used to determine the initial forces of contact. Van der Waals forces were chosen for all combinations used in this research, where cations are present to maintain charge equilibrium, to ensure the preservation of the structural formula of the compounds under investigation, and to ensure that the drug's physical or chemical properties remain unchanged [28]. There are numerous topological arrangements, each with unique benefits and drawbacks. Pore systems, for instance, can have one, two, or three-dimensional channels that, depending on the topology, allow for the reaction or entrapment of materials inside internal cages [29]. Certain metal nanoparticles may also be encapsulated in these channels[30].

The most pertinent parameters, specifically thermodynamic quantities, were employed to scrutinize the structural configurations of glucose, metformin hydrochloride, nano cinnamon, deoxyhemoglobin, and Forxiga. The analytical computations encompassed entropy, enthalpy, and Gibbs free energy, which facilitate the evaluation of the interaction strength between deoxyhemoglobin and anti-diabetic pharmaceuticals in the context of diabetes pathogenesis. Entropy, a measure of the system's unpredictability or disorder, constitutes one of the parameters of free energy, which is characterized as the amount of heat exchanged during thermodynamic processes. One can compute the Gibbs free energy as follows[31, 32]:

$$\Delta G = \Delta H - T\Delta S \quad \text{... (10)}$$

Equation 10 represents the Gibbs free energy (ΔG), enthalpy (ΔH), entropy (ΔS), and temperature (T). This process can be represented by nano cinnamon cluster docking with deoxyhemoglobin, according to the reaction rate constant[31]:

$$K(t) = Te^{-(\frac{\Delta G}{K_B T})} \quad \text{... (11)}$$

The reaction rate constant, K(t), temperature T, change in Gibbs energy, ΔG, and Boltzmann constant, K_B, are all expressed in the preceding equation.

The notion of docking has been viewed as a linked physical parameter, especially with respect to thermal stability, wherein a thorough comprehension of the pharmacological and nanostructured material dependency on cohesive energy and adsorption energy may be obtained [35]. The intrinsic electron binding energy (E_B) in this case has been evaluated for both the pre-docking and post-docking phases[33, 34]:

$$E_B = [(N\,E_X + M\,E_Y) - E_{XY}]/(N + M) \quad \text{... (12)}$$

As the energies related to interaction are computed, the residual forces acting on the surface decrease. As a result, the surface energy also decreases [35]. This is one of the processes that contributes to the exothermic properties of interaction, as the following equation illustrates[33]:

$$E_{int} = E_{Docking} - \left(E_{DHB} + E_{Drug}\right) \quad \text{... (13)}$$

Where E_B, E_{int}, $E_{Docking}$, $E_{DHB,}$ and E_{Drug}, respectively, are the binding energy, the total energies of the interaction, DHB, and the drug molecule. Also stands for the total energy required to dock DHB with the drug. The atoms in the system are represented by the letters *N* and *M*, respectively.

Materials and Computations

The research endeavor was primarily concerned with the electronic and thermodynamic parameters employed to ascertain various properties, including the energy gap, ionization potential, electron affinity, Fermi level, work function, chemical potential, electronegativity, electrophilicity index, chemical hardness, and global chemical softness, alongside considerations of entropy, enthalpy, and Gibbs free energy. Furthermore, the cohesive binding energy and the interaction energy between the pharmaceutical compound and hemoglobin were meticulously calculated. To determine the nanomaterial's potential effects on the circulatory system, docking studies with blood hemoglobin were also conducted. The heme component of hemoglobin's architecture was carefully examined in this study project. The impact of docking on the electrical and thermodynamic properties of different hypoglycemic medications is investigated using the optimized hemoglobin structure. Nano cinnamon and nano Forxiga are two nanoparticles found in these medicinal substances. In addition, electrostatic potentials are considered to explore the most advantageous features of heme docking.

The molecular architectures of hemoglobin, nano Cinnamon, Forxiga, and Glucose have been modeled and prepared utilizing the Gauss View 6.0.16 software, employing density functional theory at the B3LYP level, complemented by the 6-311G(d,p) basis set. A structural model was developed for the docking interactions between nano Cinnamon and Forxiga with Glucose. Additionally, another model was constructed for the docking interactions of deoxyhemoglobin with Glucose and/or nano Cinnamon. The subsequent simulations were conducted using Gaussian 09 software to obtain the results pertaining to the properties under investigation.

Results and Discussion

Density functional theory (DFT) has been implemented in the Gaussian 09 software suite was used for all computations, and Gauss View 6.0.16 was used for visualization. DFT is a very useful approach to explain the ground state properties of many materials, such as metals, semiconductors, insulators, and biomaterials. The electronic and thermodynamic properties were determined in this work using the B3LYP computational level in combination with the (6-311g (d,p)) basis set in all computational analyses. Natural bond order (NBO) analysis was utilized to determine the mechanism that docking the molecule structures. The optimization of molecular structures results of Deoxyhemoglobin DHB, Oxyhemoglobin OHB, nano Cinnamon, Forxiga, and Glucose are shown in **Figures 1**, **Figure 2**, and **Figure 3**, respectively.

Figures 4, **Figure 5**, and **Figure 6** depict the optimization docking process between Glucose and nano Cinnamon, the docking of Glucose with Forxiga, and the docking process between Glucose with Deoxyhemoglobin, respectively.

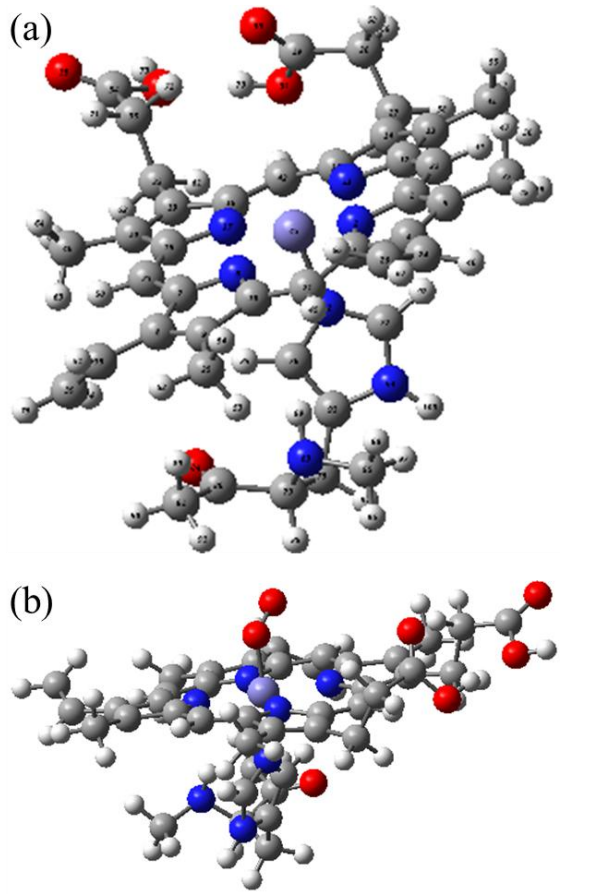

Figure 1. The optimized structure for: (a) DHB, (b) OHB.

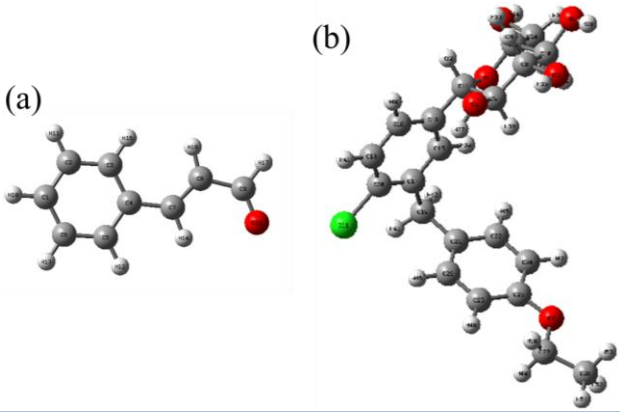

Figure 2. (a) The optimized structure of the Cinnamon molecule, (b) The optimized structure of the Forxiga molecule.

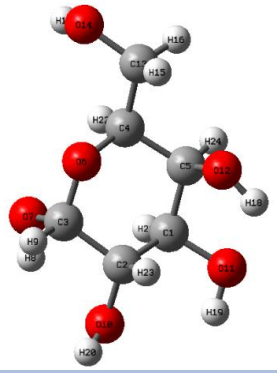

Figure 3. The optimized structure of Glucose.

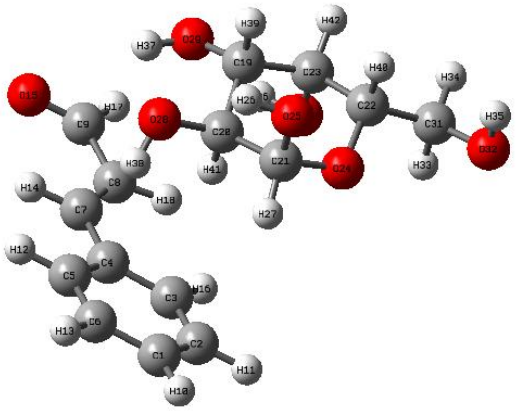

Figure 4. Docking of Glucose with nano Cinnamon.

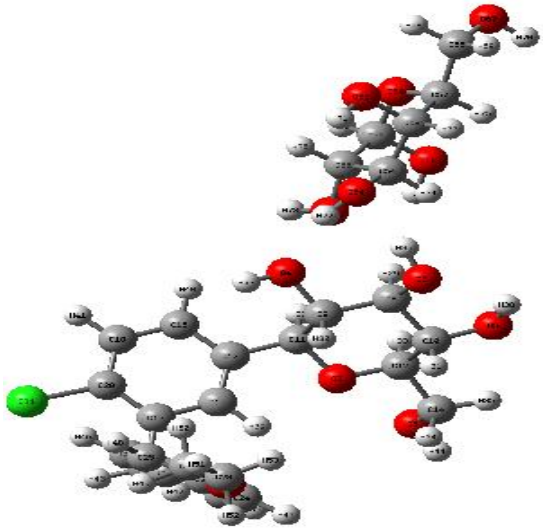

Figure 5. Docking of Glucose with Forxiga.

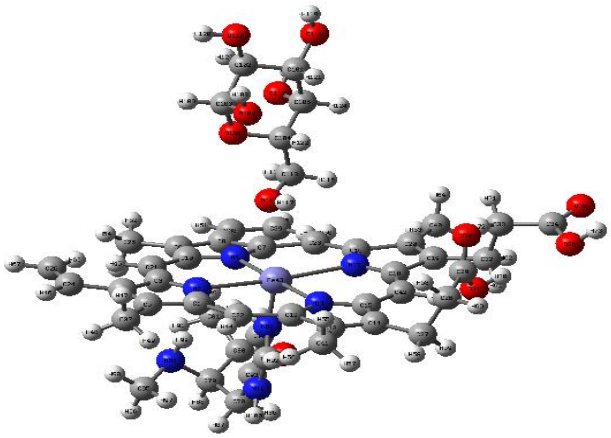

Figure 6. Docking of Glucose with deoxyhemoglobin.

The mechanism for the docking process is presented in **Table 1**. Every atom in the molecule under investigation had its natural bond arrangement (NBO) examined to ascertain the sequence in which the docking process took place between the molecules under investigation, from the highest positive charges to the highest negative charges. Vander Waals' weak bond, which aided in the docking process, was used to carry out the docking process between the molecule structures under investigation[36].

Table 1. Charges per atomic unit of charge (au) on each atom in a molecule structure as determined by Natural Bond Order (NBO) analysis.

Molecule	Positive charge (au)	Negative charge (au)
Deoxyhemoglobin	Fe = 1.3	-
Nano Cinnamon	C = 0.187	O = 0.298
Forxiga	C = 1.832	O = 0.422
Glucose	C = 0.258	O = 0.428

The electronic properties were calculated through the results of the optimal structures, which were presented in Figures 1 to 7, and for all structures and dockings. **Table 2** shows the results of the electronic properties of the basic materials used in the study.

Table 2. The electronic properties in (eV).

Properties	Deoxyhemoglobin	Glucose	Forxiga	Nano Cinnamon
HOMO	-4.780	-7.177	-6.00	-6.716
LUMO	-1.945	0.1463	-0.805	-2.378
IP	4.78	7.177	6.003	6.716
EA	1.945	-0.146	0.805	2.378
E_g	2.835	7.324	5.198	4.337
E_F	-3.363	-3.515	-3.404	-4.547
Φ_m	1.417	3.662	2.599	2.168
χ	3.363	3.515	3.404	4.547
η	1.417	3.662	2.599	2.168
ζ	0.352	0.136	0.192	0.23
ω	3.989	1.687	2.229	4.767
SCF	-3651.661	-687.407	-1727.276	-423.115

After determining which pharmacological agents are the most effective in treating hyperglycemia, research will be done on glucose, the primary cause of hyperglycemia, and then a molecular docking analysis will be performed with the chosen pharmacological agent to determine the drug's therapeutic efficacy in quickly controlling hyperglycemia. Moreover, for each pharmacological agent, a further docking study will be conducted for the hemoglobin and glycemic parameters in order to determine the degree of these agents' physiological effects on the human body, as well as their possible toxicity.

The results in **Table 3** concerning the electronic properties can be explained by the hemoglobin structure; the Iron ion located in the middle of the porphyrin is associated with deoxyhemoglobin ($C_{42}H_{45}FeN_7O_7$)[37]. Moreover, along its fourth axis, the molecular entity ($C_{34}H_{31}N_4O_6$) is docking with an imidazole acetate molecule ($C_8H_{14}N_3O$). Deoxyhemoglobin has a broad range of chemical affinities. The way that glucose interacts with different antidiabetic pharmaceutical agents (such as Forxiga and nano-cinnamon) has led to the identification of the best drug for a given patient. Apart from the contacts between hemoglobin and nano-cinnamon, there is also a parallel docking relationship between glucose and nano-cinnamon. Forxiga and nano-cinnamon applied together offer a potential treatment strategy for the treatment of diabetes.

Data about the relationship between glucose and anti-diabetic pharmaceutical medicines (i.e., nano cinnamon and Forxiga) are presented in **Table 4**, which shows that the Gibbs' free energy reaction is non-spontaneous before and after the docking process. However, during the docking process, Gibbs free energy increases significantly, especially for the glucose-Forxiga contact and the glucose-nano-cinnamon interaction. Since every reaction has exothermic properties, the enthalpy considerations imply that thermal energy is released prior to and following the fusion at every step. Moreover, all of the reaction's entropy values are positive as the binding energies of the final products are greater than those of the reactants[31].

Table 3. The electronic properties in (eV) for docking reactions.

Properties	Glucose with DHB	Glucose/nano Cinnamon	Glucose / Forxiga
HOMO	-4.8977	-7.077	-6.086
LUMO	-2.5148	-2.725	-0.963
IP	4.8977	7.0778	6.086
EA	2.5148	2.725	0.963
E_g	2.3828	4.351	5.123
E_f	-5.1787	-4.901	-3.525
Φ_m	3.9374	2.175	2.561
χ	5.1787	4.901	3.525
η	3.9374	2.175	2.561
ζ	0.1269	0.229	0.195
ω	3.4057	5.521	2.425
SCF	-118052.43	-1110.540	-2414.708

Consequently, one may deduce that nano Cinnamon represents the most efficacious therapeutic agent for the swift amelioration of glycemic dysregulation; Forexiga demonstrates effectiveness and promptness as well, although not as expeditiously as nano Cinnamon. This conclusion is consistent with the findings presented in the study [38, 39].

Also, it can be noticed from Table 4 that the lowest energy binding occurs before docking, especially for the Glucose and nano Cinnamon molecule. After the docking process, the energy correlation increases. Since Glucose with Forxiga has higher binding energies than Glucose docking with nano Cinnamon. After the docking process, the adsorption energy was found to be more stable. Compared to Glucose with nano Cinnamon and Glucose with Forxiga, the adsorption energy of Glucose with nano Cinnamon was more stable and exothermic interaction[40].

Table 4. Gibbs energy and its components (enthalpy and entropy) are compared with the binding and interaction energies under standard conditions.

Energies (eV)	Nano Cinnamon	Forxiga	Glucose	Glucose / nano Cinnamon	Glucose / Forxiga
G	2.947	10.158	4.3617	7.810	15.221
H	4.148	12.529	5.738	9.954	18.294
ST	1.196	2.361	1.371	2.136	3.061
ΔG	-	-	-	0.500	0.701
ΔH	-	-	-	0.067	0.027
ΔST	-	-	-	-0.431	-0.671
E_B	6.068	-663.882	5.383	-2977.787	-8953.155
E_{int}	-	-	-	-0.481	-35488.186

Prior to the molecular docking process, **Table 5** illustrates that the Gibbs free energy associated with each molecule indicates a non-spontaneous interaction. Furthermore, it is noteworthy that deoxyhemoglobin exhibits the highest Gibbs free energy, succeeded by glucose and nano cinnamon. It has been established that all energies result in heat release in the context of enthalpy, which is congruent with the observation that entropy is also positive, given that the energy of the products surpasses that of the reactants[41].

Table 5. Compares the molecules under study's Gibbs energy and its components, enthalpy, and entropy, prior to the docking procedure.

Energies (eV)	Nano Cinnamon	Forxiga	Glucose	DHB
G	2.947	10.158	4.361	19.525
H	4.148	12.529	5.738	23.485
ST	1.196	2.361	1.371	3.945

Table 6 shows the thermodynamic properties of deoxyhemoglobin docked with three substances: nano Cinnamon, glucose, and Forxiga. The data of enthalpy indicates that the reactions release heat and have a higher entropy energy state for the products compared to the reactants. However, none of the reactions are spontaneous[42, 43]. Table 6 illustrates that the interaction of deoxyhemoglobin with Glucose and Forxiga induces a spontaneous alteration in Gibbs free energy, while the interaction of deoxyhemoglobin with nano Cinnamon does not exhibit spontaneity. Furthermore, all reactions are characterized as endothermic according to the evaluation of enthalpy changes.

Table 6. Compares the binding and interaction energies of particles under standard conditions with the Gibbs energy and its components (enthalpy and entropy) for molecules docking to deoxyhemoglobin.

Energies (eV)	Nano Cinnamon with deoxyhb	Glucose with DHB	Forxiga with DHB
G	22.965	19.677	29.764
H	26.571	23.739	34.075
ST	3.592	4.047	4.295
ΔG	0.492	-4.209	0.581
ΔH	-1.063	-5.484	-0.991
ΔST	-1.549	-1.269	-1.573
E_B	5.872	-26.739	-25.778
E_{int}	16.591	17.990	-3.177

Because the reactant energy is higher than the product energy in both the deoxyhemoglobin and glucose processes, the entropy is negative. On the other hand, docking deoxyhemoglobin with Forxiga is beneficial. Therefore, it may be concluded that although glucose harms the bloodstream of humans, nano cinnamon and Forxiga both interact with deoxyhemoglobin and are safe. The amount of energy required to break each bond is shown in Table 6. Due to the heat-emitting binding energy, the docking of deoxyhemoglobin with nano Cinnamon, Forxiga, and glucose is more stable. To be clear, the deoxyhemoglobin docking is more stable because of the energy involved in the contact and adsorption. When docking deoxyhemoglobin with nano Cinnamon and Forxiga, they are unstable.

Table 6 presents a comparative analysis of the Gibbs energies associated with Glucose in conjunction with Forxiga and nano Cinnamon. Moreover, all Gibbs free energies are associated with an exothermic reaction that lacks spontaneity, with a significantly elevated Gibbs free energy noted when Glucose is complexed with both nano Cinnamon and Forxiga. The computations illustrated in Table 6 further indicate that, within the context of Gibbs free energy variation, the docking of Forxiga with Glucose and the docking of Forxiga with nano Cinnamon demonstrate a reductive and endothermic behavior, whereas the docking interactions involving Forxiga with Glucose and the combination of Forxiga, nano Cinnamon, and Glucose reveal a non-spontaneous exothermic reaction[38, 44, 45].

As a result, it is possible to determine the efficacy of Forxiga when combined with the herbal remedy of nano Cinnamon, even if the Gibbs free energy resulting from the docking of Glucose to Forxiga is significantly altered. This occurrence can be attributed to Forxiga's ability to form a strong bond with Glucose, which makes it easier for nano Cinnamon to quickly alleviate hyperglycemic situations[46]. This claim is demonstrated when the docking processes of Glucose with nano Cinnamon and Glucose with Forxiga are compared. **Table 7** lists the metrics that include binding energy and interaction energy. Due to its exothermic nature, the binding energy between nano Cinnamon and Glucose is more stable; however, the docking energy of Glucose with respect to both nano Cinnamon and Forxiga is unstable.

Table 7. Comparing the binding and interaction energies of particles under standard conditions with Gibbs energy and its components (enthalpy and entropy) for molecules docking to glucose.

Energies (eV)	Glucose with nano Cinnamon.	Glucose with Forxiga	Forxiga with nano Cinnamon	Forxiga with nano Cinnamon and Glucose
G	7.810	15.221	13.612	18.520
H	9.954	18.294	16.675	22.384
ST	2.136	3.072	3.062	3.863
ΔG	0.500	0.701	0.505	0.546
ΔH	0.067	0.027	-0.002	-0.029
ΔST	-0.431	-0.674	-0.508	-0.575
E_B	5.688	5.605	21620.189	-20367.434
E_{int}	-0.481	-65706.622	-65498.896	-110862.159

Conclusion

About the glycemic disorder that constituted the focal point of the investigation, and contingent upon a series of molecular docking analyses of the pharmacological agents implicated in this pathology, alongside deoxyhemoglobin, numerous deductions can be drawn from the docking studies involving Glucose with deoxyhemoglobin, Glucose with nano Cinnamon, and Glucose with Forxiga. The primary methodologies employed for molecular docking include the natural bond ordering (NBO) computations, which elucidate the highest positive and negative charge distributions on both interacting biochemical entities. The assessment of electronic and thermodynamic parameters substantiated the assertion that nano Cinnamon represents the most efficacious herbal intervention.

As a result, even if there is a significant change in Gibbs free energy upon the binding of Glucose to Forxiga, Forxiga can be trusted to help in the natural herbal treatment of nano Cinnamon. This is because Forxiga can form a strong bond with Glucose, which accelerates the removal of blood sugar disorders by nano Cinnamon. The deoxyhemoglobin docking with Glucose and Forxiga results in a spontaneous shift in Gibbs free energy, but not with nano Cinnamon, as can be seen by comparing the docking processes of Glucose and Forxiga. In addition, the measurement of enthalpy change implies that all reactions are endothermic. For both the

Glucose and deoxyhemoglobin metabolic processes, the entropy is shown to be negative since the energy of the reactants is greater than the energy of the products. On the other hand, it is thought to be advantageous for deoxyhemoglobin to interact with Forxiga. Consequently, it can be concluded that although Forxiga and nano Cinnamon interact with deoxyhemoglobin and are considered non-toxic, Glucose negatively impacts the human body's circulatory system.

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Declaration of Competing Interests

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