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Antiviral ribavirin binding to human serum albumin in diabetes and uraemia: A molecular docking study

Fahad M. Almutairi, Mohammad Rehan Ajmal*

Physical Biochemistry Research Laboratory, Department of Biochemistry, Faculty of Science, University of Tabuk, Tabuk 71491, Saudi Arabia

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Abstract

Human Serum Albumin (HSA) is abundant plasma protein in human blood. It plays a critical role in the transport and distribution of endogenous and exogenous compounds. Protein binding affects free fraction of a drug thus affecting pharmacokinetics and therapeutic efficacy. Glycation of HSA under diabetic conditions and the accumulation of uremic toxins in uraemia may alter drug–protein interactions. Therefore, the present study aimed to investigate the binding interactions of ribavirin and selected uremic toxins with binding interactions involving glycation-sensitive HSA residues using molecular docking analysis. Molecular docking results demonstrated that ribavirin bind to HSA with hydrogen bonding and hydrophobic interactions. Key glycation-prone residues, including ARG222, ARG218, and LYS195, were identified at the ribavirin binding site. Several of these residues were also involved in the binding of uremic toxins, indicating potential competition for ligand binding in diabetic and uremic conditions. The overlap of interaction sites suggests that glycation and toxin accumulation may influence the structural and biochemical properties of HSA, thereby affecting ribavirin binding affinity and distribution. In conclusion, this study highlights the important role of glycation-sensitive HSA residues in mediating ribavirin and uremic toxin interactions. These insights may support the future design and optimization of ribavirin-based therapeutics.

Keywords: Human serum albumin, ribavirin, uremic toxins, molecular docking, binding interaction.

1. Introduction

Human serum albumin (HSA) is major transport carrier plasma protein in human blood[1]. It has high binding capacity and multiple binding regions mainly known as Sudlow sites I and II on HSA molecule. These binding regions play key role in determining how drugs are distributed in the body, how long they stay in circulation, and how they behave pharmacokinetically. When drugs bind to albumin, only the unbound (free) portion is pharmacologically active, while the bound portion serves as a reservoir that helps maintain stable drug levels in the bloodstream. Thus drug binding changes may occur due to changes in albumin structure due to physicochemical alterations in blood [2]. It may impact effectiveness and safety of drugs. Ribavirin is a broad-spectrum antiviral nucleoside analogue used to treat several viral infections. Compared to many strongly protein-bound drugs, ribavirin binding is moderate to HSA, mainly through hydrogen bonding and electrostatic interactions. This means a relatively large fraction of the drug remains free in plasma, contributing to its antiviral activity. However, disease conditions such as diabetes mellitus and chronic kidney disease (CKD) can alter albumin's structure and, in turn, affect how drugs interact with it. Diabetes mellitus is one of the leading causes of CKD worldwide. In long-standing high blood sugar conditions, proteins like albumin undergo non-enzymatic glycation, leading to the formation of advanced glycation end products (AGEs). In advanced kidney disease, additional changes occur, including carbamylation, oxidative stress, and accumulation of uremic toxins [3,4]. Together, these processes can change the shape, suppleness, and chemical properties of transport proteins, especially in drug binding domains that contain lysine and arginine residues. Uremic toxins such as indoxyl sulfate and p-cresyl sulfate may also compete with drugs for the same binding sites, further reducing binding affinity [5,6]. These structural modifications can lead to increasing the free fraction of drugs in the blood affecting both therapeutic response and the risk of toxicity. Understanding how antiviral drug interact with albumin is therefore important for improving treatment strategies in these patient groups.

In this study, we aimed to explore the molecular interaction between ribavirin and HSA and compare its binding behaviour with common uremic toxins using molecular docking approach. This approach helps to better understand how diabetes- and uraemia-related changes may

* Corresponding author.
E-mail address: mkhan@ut.edu.sa (M. R. Ajmal).
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influence drug binding and pharmacokinetics as glycation prone residues take part in interaction process of drug with protein.

2. Materilas and Methods

2.1. Protein and Ligand Preparation

The three-dimensional crystal structure of Human Serum Albumin (HSA) was obtained from the Protein Data Bank (PDB ID: 1AO6) [7]. Ligand structures, including ribavirin and selected uremic toxins, were retrieved from PubChem in SDF format (PubChem IDs are given in Table 1) and subsequently converted into the appropriate file formats required for molecular docking. Molecular docking simulations were performed using AutoDock 4.2.0 software (http://autodock.scripps.edu). A grid calculation was performed to cover all active site residues, with grid dimensions set at 126 × 126 × 126 points along the X, Y, and Z axes. AutoDock rigid parameters were set for protein chains, while the ligand was allowed flexible rotation to obtain possible binding conformations. The Lamarckian genetic algorithm (LGA) was selected with a GA population size of 150 and a maximum number of 2,500,000 energy evaluations. The lowest energy conformation of the largest cluster from each docking simulation was extracted and analyzed. The 10 best solutions based on docking score were retained for further analysis. The grid center coordinates were defined based on the localization of the binding pockets or values reported in previous literature (insert X, Y, Z center coordinates here). For each ligand, multiple binding poses were generated, and the conformation with the lowest binding energy within the most populated cluster was selected for further analysis. Docked conformations were visualized with Discovery Studio 3.5 visualizer [8,9].

2.2. Data Analysis and Visualization

The top 10 docking poses, based on the lowest energy-ranked docking pose, were selected for detailed interaction analysis [10]. Key protein–ligand interactions, including hydrogen bonds, hydrophobic contacts, and electrostatic interactions, were examined to identify important amino acid residues involved in binding within Sudlow site I and Sudlow site II. The final docked complexes were visualized and analyzed.

3. Results

Molecular docking was performed to elucidate the binding mode of ribavirin with human serum albumin (HSA). The docking results revealed that ribavirin binds within the binding pocket of HSA with a moderate binding energy of -5.23 kcal/mol (Table 3). Analysis of the docked complex showed that ribavirin interacts with several amino acid residues, including CYS448, LYS436, ASP451, TYR452, SER454, TRP214, LEU198, LYS195, ALA191, and VAL445. The binding is primarily stabilized by hydrogen bonding and electrostatic interactions, along with hydrophobic contacts. Notably, glycation-prone residue LYS195 was found to be involved in the binding interaction. The binding pose and interaction pattern of ribavirin with HSA are illustrated in Figure 1.

HSA is important in drug transport, interaction of HSA with antiviral drug ribavirin has studied[11,12] it interacts with moderate binding energy (Table 3), amino acid residues at the binding site include CYS448, LYS436, ASP451, TYR452, SER454, TRP214, LEU198, LYS195, ALA191, VAL445 residues, electrostatic and hydrogen bonding are major interaction forces in binding interaction as shown in Figure 1. Interesting observation here is that ribavirin shares most of the binding site residues in common with uremic toxins as shown in Table 1 and glycation prone residue Lys195 is also found to be involved in binding interaction of ribavirin with HSA as listed in and Table 2.

Interaction of 2-hydroxycinnamic acid (o-coumaric acid) with HSA was also investigated using molecular docking. As shown in Table 3, 2-hydroxycinnamic acid binds to HSA with a moderate binding energy of -6.24 kcal/mol. The docking analysis revealed that this uremic toxin interacts with several amino acid residues, including SER454, LYS199, ARG218, TRP214, LYS195, LEU198, VAL343, and ASP451 (Table 2). Interestingly, five of these residues are common with the ribavirin binding site, indicating a significant overlap in binding regions. Furthermore, glycation-prone residues such as LYS195 and ARG218 were found to be involved in the interaction. These findings suggest that the binding of 2-hydroxycinnamic acid may be affected by glycation, and the presence of this toxin could potentially alter ribavirin binding. The detailed binding mode and interaction profile are presented in Figure 2.

CMPF (3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid) is a uremic toxin that exhibits reduced renal clearance and strong albumin binding, making it poorly removable by standard dialysis [13,14]. Molecular docking analysis revealed that CMPF binds to HSA with a relatively strong binding energy of -7.11 kcal/mol (Table 3), which is the highest among the toxins examined in this study. The binding interaction involves amino acid residues TYR452, VAL455, TRP214, LEU198, LYS199, ASP451, ARG218, and LYS195 (Table 2). Hydrophobic and electrostatic interactions play major roles in stabilizing the protein–ligand complex. Notably, CMPF shares five common residues with the ribavirin binding site, and glycation-prone residues such as LYS195 and ARG218 are also involved in its binding. These observations indicate that hypergly-

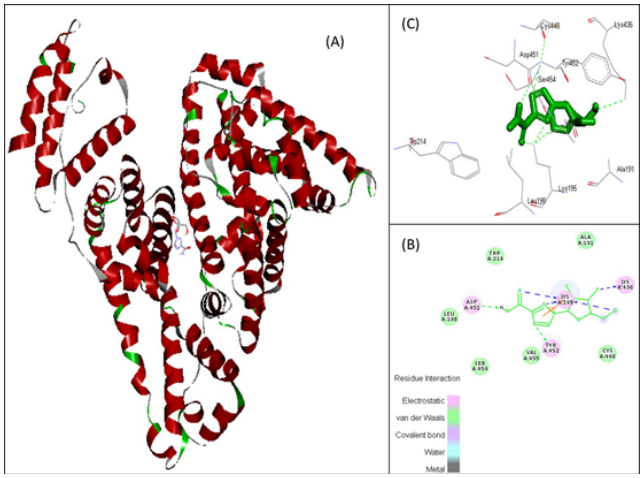


Fig. 1. Molecular docking of Ribavirin with HSA (A) Ribavirin bound to HSA. HSA is represented using ribbon and Ribavirin, Ribavirin is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of Ribavirin with HSA. (C) 3D representation of interactions of Ribavirin with the residues of HSA in the binding pocket of HAS.

Table 1. List of uraemia toxins considered in the study.

	Compound CID	IUPAC Name	interaction
2-hydroxycinnamic acid	637540	(E)-3-(2-hydroxyphenyl)prop-2-enoic acid	Electrostatic, van der Waals, H-bonding interaction
Cmpfpa	123979	2-(2-carboxyethyl)-4-methyl-5-propylfuran-3-carboxylic acid	Electrostatic, van der Waals, H-bonding interaction
hydroxybenzoic acid	135	4-hydroxybenzoic acid	Electrostatic, van der Waals, H-bonding interaction
p-hydroxyphenylacetic acid	135	2-(4-hydroxyphenyl)acetic acid	Electrostatic, van der Waals, H-bonding interaction
hippuric acid	464	2-benzamidoacetic acid	Electrostatic, van der Waals, H-bonding interaction
indoleacetic acid	802	2-(1H-indol-3-yl)acetic acid	Electrostatic, van der Waals, H-bonding interaction
indoxyl sulfate	10258	1H-indol-3-yl hydrogen sulfate	Electrostatic, van der Waals, H-bonding interaction
ribavirin	37542	1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,2,4-triazole-3-carboxamide	Electrostatic, van der Waals, H-bonding interaction

Table 2. Common residues that uraemia toxins share with ribavirin as obtained from molecular docking results.

molecule	binding site residues of molecules	number of common residues with ribavirin binding site
ribavirin	CYS448, LYS436, ASP451, TYR452, SER454, TRP214, LEU198, LYS195, ALA191, VAL445	2 non common aa with any of the toxin
2-hydroxycinnamic acid	SER454, LYS199, ARG218, TRP214, LYS195, LEU198, VAL343, ASP451	5 common residues
Cmpfpa	TYR452, VAL455, TRP214, LEU198, LYS199, ASP451, ARG218, LYS195	5 common residues
hydroxybenzoic acid	VAL344, VAL343, SER454, VAL455, TRP214, LYS195, ASP451, LEU198, LYS199	5 common residues
p-hydroxyphenylacetic acid	ASP187, LYS436, TYR452, ALA191, ALA194, VAL455, LYS432, LYS190, ASN429, GLU459, VAL456	3 common residues
hippuric acid	ARG222, VAL343, ARG218, LYS195, ASP451, LEU198, TRP214, SER454	4 common residues
indoleacetic acid	ARG218, ASP451, LEU198, TRP214, VAL343, LYS195, VAL455, SER454	5 common residues
indoxyl sulfate	GLU292, ARG218, LYS195, LYS199, ALA291, ARG222, TRP214, LEU238	2 common residues

caemic conditions may affect the transport and binding of CMPF, and conversely, the presence of this toxin could potentially interfere with ribavirin binding. The docking pose and interaction details are illustrated in Figure 3.

4-Hydroxybenzoic acid is a phenolic compound that accumulates in chronic kidney disease (CKD) due to reduced renal clearance and increased gut microbial production [15]. Molecular docking analysis revealed that this uremic toxin binds to HSA with a moderate binding energy of -5.49 kcal/mol (Table 3). The binding interaction involves amino acid residues VAL344, VAL343, SER454, VAL455, TRP214, LYS195, ASP451, LEU198, and LYS199 (Table 2). Hydrogen bonding and electrostatic interactions are the major forces contributing to binding. Notably, five residues are common with the ribavirin binding site, and glycation-prone residues such as LYS195 are also involved in the interaction. These findings suggest that hyperglycaemia may affect the transport of 4-hydroxybenzoic acid, and the accumulation of this toxin could potentially alter the binding affinity of ribavirin to

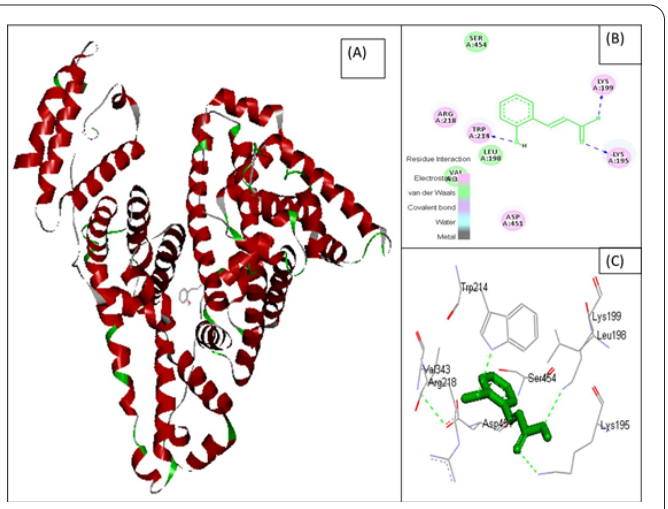


Fig. 2. Molecular docking of 2-hydroxycinnamic acid with HSA (A) 2-hydroxycinnamic acid bound to HSA. HSA is represented using ribbon and 2-hydroxycinnamic acid is shown in stick model. (B) 2D interaction diagram showing the polar and hydrophobic interactions of 2-hydroxycinnamic acid with HSA. (C) 3D representation of interactions of 2-hydroxycinnamic acid with the residues of HSA in the binding pocket of HAS.

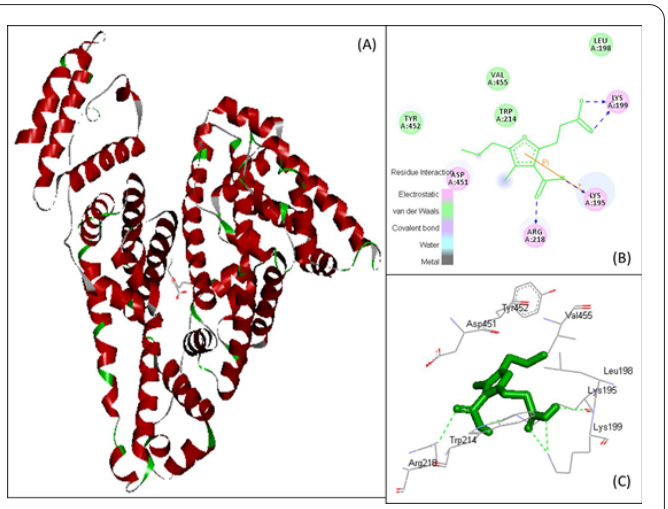


Fig. 3. Molecular docking of 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid with HSA (A)-3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid bound to HSA. HSA is represented using ribbon and 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid with HSA. (C), 3D representation of interactions of 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid with the residues of HSA in the binding pocket of HAS.

HSA. The detailed binding mode and interaction pattern are presented in Figure 4.

4-Hydroxyphenylacetic acid (4-HPAA) is a tyrosine-derived microbial and host metabolite that accumulates in chronic kidney disease (CKD) due to reduced renal clearance and impaired tubular secretion [16]. CKD-related gut dysbiosis may further increase its production. Molecular docking analysis revealed that 4-HPAA interacts with HSA with a moderate binding energy of -6.25 kcal/mol (Table 3). The binding interaction involves amino acid residues ASP187, LYS436, TYR452, ALA191, ALA194, VAL455, LYS432, LYS190, ASN429, GLU459, and VAL456 (Table 2). Among these, three residues (LYS436, TYR452, and ALA191) are common with the ribavirin binding site. Glycation-prone residues were also found to be involved in the binding interaction. These observations suggest that the presence of this toxin in kidney malfunction could potentially contribute to ribavirin binding defects. The docking pose and interaction details are illustrated in Figure 5.

Hippuric acid is a glycine conjugate of benzoic acid that is normally cleared efficiently by the kidneys. In chronic kidney disease (CKD), reduced glomerular filtration and impaired tubular secretion cause its accumulation in the blood [17]. Increased gut microbial production of benzoic acid precursors further contributes to elevated levels. As a protein-bound uremic toxin, hippuric acid promotes oxidative stress, endothelial dysfunction, and inflamma-

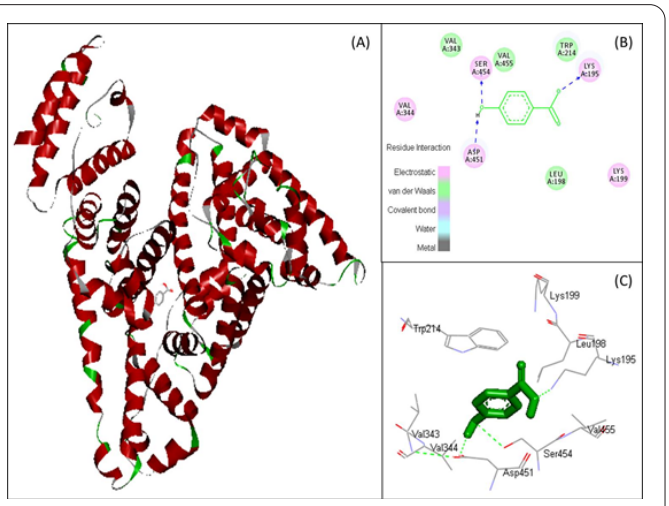


Fig. 4. Molecular docking of 4-hydroxybenzoic acid with HSA (A)-4-hydroxybenzoic acid bound to HSA. HSA is represented using ribbon and 4- hydroxybenzoic acid is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of 4-hydroxybenzoic acid with HSA. (C), 3D representation of interactions of 4-hydroxybenzoic acid with the residues of HSA in the binding pocket of HAS.

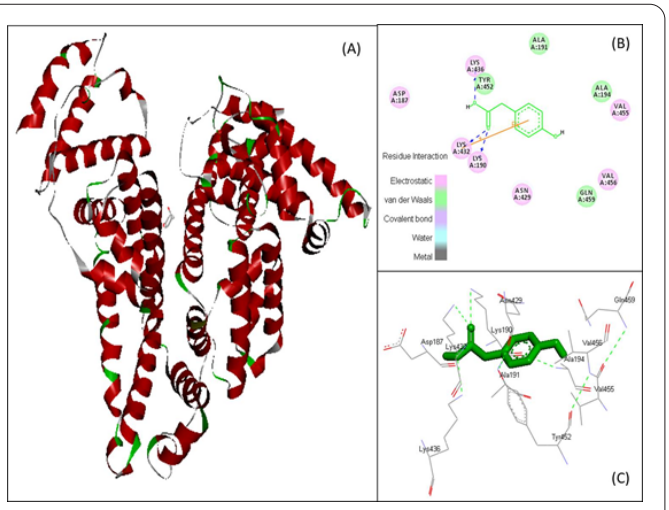


Fig. 5. Molecular docking of 4-hydroxyphenylacetic to HSA (A)-4-hydroxyphenylacetic acid bound to HSA. HSA is represented using ribbon and 4-hydroxyphenylacetic acid is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of 4-hydroxyphenylacetic acid with HSA. (C), 3D representation of interactions of 4-hydroxyphenylacetic acid with the residues of HSA in the binding pocket of HAS.

tion. Molecular docking analysis revealed that hippuric acid binds to HSA with a moderate binding energy of -6.84 kcal/mol (Table 3). The binding interaction involves amino acid residues ARG222, VAL343, ARG218, LYS195, ASP451, LEU198, TRP214, and SER454 (Table 2). Hydrogen bonding and electrostatic interactions are the major forces contributing to binding. Notably, four common residues are shared with the ribavirin binding site, and glycation-prone residues such as LYS195, ARG218, and ARG222 are involved in the interaction. These observations suggest that the binding of hippuric acid may affect the binding of the antiviral drug ribavirin, and hyperglycaemic conditions could also influence the binding of this uremic toxin. The detailed binding mode and interaction pattern are presented in Figure 6.

Indole-3-acetic acid (IAA) is a tryptophan-derived metabolite that is normally cleared by the kidneys. In chronic kidney disease (CKD), reduced filtration and tubular secretion cause its accumulation, further amplified by gut dysbiosis that increases indole production from dietary tryptophan [18]. As a uremic toxin, elevated IAA promotes oxidative stress, inflammation, endothelial dysfunction, and aryl hydrocarbon receptor (AhR) activation, contributing to cardiovascular risk and CKD progression. Molecular docking analysis revealed that IAA binds to HSA with a moderate binding energy of -6.27 kcal/mol (Table 3). The binding interaction involves amino acid residues ARG218, ASP451, LEU198, TRP214, VAL343, LYS195, VAL455, and SER454 (Table 2). Hydrogen bonding and electrostatic interactions are the major forces contributing to binding. Notably, five common residues are shared with the ribavirin binding site, and glycation-prone residues such as LYS195 and ARG218 are involved in the interaction. These findings indicate possible altered transport effects in hyperglycaemia and chronic kidney diseases. The docking pose and interaction details are illustrated in Figure 7.

Indoxyl sulfate (IS) is a protein-bound uremic toxin produced from gut bacterial metabolism of tryptophan to indole, which is then converted in the liver to indoxyl sulfate and normally excreted by the kidneys [19]. In chronic kidney disease (CKD), reduced filtration and tubular secretion lead to its accumulation, further amplified by gut dysbiosis increasing indole production. IS is strongly albumin-bound, making it poorly dialyzable, and contributes to oxidative stress, inflammation, endothelial dysfunction, and renal fibrosis, thereby worsening cardiovascular and renal outcomes. Molecular docking analysis revealed that indoxyl sulfate binds to HSA with a binding energy of -6.90 kcal/mol (Table 3). The binding interaction involves amino acid residues GLU292, ARG218, LYS195, LYS199, ALA291, ARG222, TRP214, and LEU238 (Table 2). Hydrogen bonding and electrostatic interactions were found to be the major forces of interaction. Notably, IS shares two common amino acid residues with the ribavirin binding site, and glycation-prone residues such as LYS195, ARG218, and ARG222 are involved in the binding interaction. This observation indicates the possibility of altered binding in hyperglycaemia and chronic kidney disease. The docking pose and interaction details are illustrated in Figure 8.

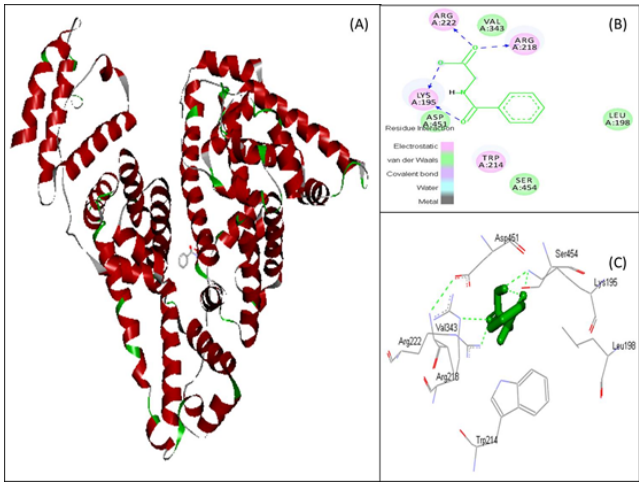


Fig. 6. Molecular docking of hippuric acid bound to HSA (A)-hippuric acid bound to HSA. HSA is represented using ribbon and hippuric acid is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of hippuric acid with HSA. (C), 3D representation of interactions of hippuric acid with the residues of HSA in the binding pocket of HAS.

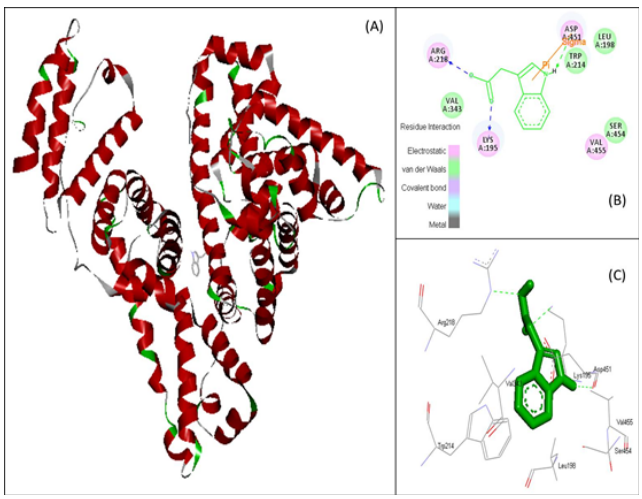


Fig. 7. Molecular docking of indoleacetic acid bound to HSA (A)-indoleacetic acid bound to HSA. HSA is represented using ribbon and indoleacetic acid is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of indoleacetic acid with HSA. (C), 3D representation of interactions of indoleacetic acid with the residues of HSA in the binding pocket of HSA.

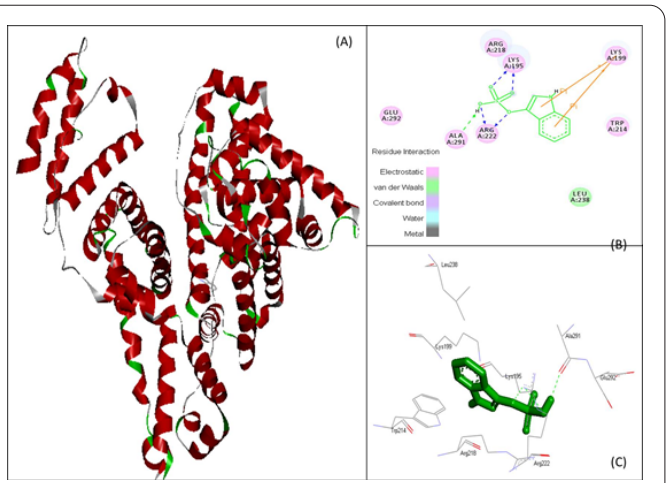


Fig. 8. Molecular docking of indoxyl sulfate bound to HSA (A)-indoxyl sulfate bound to HSA. HSA is represented using ribbon and indoxyl sulfate indoxyl sulfate is shown in stick model, (B) 2D interaction diagram showing the polar and hydrophobic interactions of indoxyl sulfate with HSA. (C), 3D representation of interactions of indoxyl sulfate with the residues of HSA in the binding pocket of HAS.

Table 3. Free energy of binding interaction of various molecules employed in study.

molecule	Compound CID	IUPAC Name	Free energy of binding interaction
Ribavirin	36791	1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,2,4-triazole-3-carboxamide	-5.23
2-hydroxycinnamic acid	637540	(E)-3-(2-hydroxyphenyl)prop-2-enoic acid	-6.24
Cmpfpa	123979	2-(2-carboxyethyl)-4-methyl-5-propylfuran-3-carboxylic acid	-7.11
hydroxybenzoic acid	135	4-hydroxybenzoic acid	-5.49
p-hydroxyphenylacetic acid	135	2-(4-hydroxyphenyl)acetic acid	-6.25
hippuric acid	464	2-benzamidoacetic acid	-6.84
indoleacetic acid	802	2-(1H-indol-3-yl)acetic acid	-6.27
indoxyl sulfate	10258	1H-indol-3-yl hydrogen sulfate	-6.9

4. Discussion

Molecular docking is a computational method used to predict how drug molecules bind to proteins such as Human Serum Albumin (HSA), the main transport protein in blood plasma. It is important tool to study binding orientation and interaction of drug molecules and identifies key amino acid residues involved and interaction forces involved in binding interactions. The recurrence of common residues in different ligand-binding sites suggests that they play a crucial role in maintaining structural complementarity and stabilizing protein–ligand complexes across diverse molecular systems. When these residues are shared among multiple ligands or binding partners, competitive or cooperative interactions may occur, potentially altering ligand-binding affinity and specificity. Such interactions can influence molecular transport affecting the absorption, distribution, metabolism, and excretion of compounds. Consequently, the simultaneous presence of molecules targeting similar binding residues may modify transport efficiency and pharmacokinetic behavior, leading to altered bioavailability, efficacy, or toxicity profiles. In chronic hyperglycaemia, elevated glucose leads to non-enzymatic glycation of human serum albumin (HSA), especially at lysine and arginine residues such as Lys195, Lys199, Arg218, and Arg222. This can progress from early glycation products (Amadori products) to advanced glycation end products (AGEs), causing structural and conformational changes in albumin. These modifications may distort drug-binding and alter conformation, and reduce binding flexibility, thereby decreasing HSA affinity for many drugs. As a result, the free fraction and protein-bound drug may change, raising the risk of toxicity despite normal total plasma levels. Molecular docking interaction of uremic toxins with human serum albumin indicated overlapping in amino acid residues in binding region, also glycation prone residues are also found to involve in binding interaction nad can be implicated in altered binding in hyperglycaemia states. Additional factors in diabetes and chronic kidney disease such as oxidative stress, carbamylation, and hypoalbuminemia can further impair binding. Although ribavirin has relatively low-to-moderate protein binding, altered HSA structure plus reduced renal clearance in disease states may still increase its free fraction and exposure, contributing to adverse effects like hemolytic anemia. Overall, HSA glycation in diabetes can significantly impact drug pharmacokinetics and may require closer therapeutic monitoring and dose adjustment in affected patients.

5. Conclusion

In chronic kidney disease (CKD), reduced glomerular filtration and impaired tubular secretion lead to the progressive accumulation of uremic toxins in the blood. Additional contributions come from altered gut microbiota and metabolic factors such as high protein intake. Many of these uremic toxins are protein-bound and accumulate because they are poorly cleared by the kidneys, among studied toxins CMPFA has strongest binding (Table 3). Binding of toxin can alter the local binding environment for other molecules, At the same time, chronic hyperglycaemia promotes glycation of proteins like HSA, the main plasma protein responsible for transporting hormones, fatty acids, and drugs. Both glycated HSA and uremic toxins can alter albumin structure and compete for binding sites, reducing its ligand-binding capacity. Together, these changes increase the free fraction of circulating drugs, potentially causing altered pharmacokinetics, reduced efficacy, and higher risk of toxicity. This interaction is clinically important in CKD management, highlighting the need for glycaemic control and strategies to reduce uremic toxin burden, such as dialysis or oral adsorbents. These computational predictions require experimental validation using biophysical methods such as fluorescence spectroscopy or isothermal titration calorimetry.

Competing Interests

The authors declare no competing interests

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Use of Artificial Intelligence Tools

Some sentences in this manuscript were revised with the assistance of artificial intelligence, based language models to improve clarity and readability. All intellectual content, interpretations, and conclusions are solely the responsibility of the authors.

References

1. Baig MH, Gupta P, Khan MI, Alajmi MF, Hussain A, Hassan MI, Dong JJ (2022) Probing the Interaction of Selonsertib with Human Serum Albumin: In silico and In vitro Approaches. Curr Top Med Chem 22(10): 879–890 doi: 10.2174/1568026622666220330012032
2. Leboffe L, di Masi A, Polticelli F, Trezza V, Ascenzi P (2020) Structural Basis of Drug Recognition by Human Serum Albumin. Curr Med Chem 27: 4907–4931 doi: 10.2174/0929867326666190320105316
3. Wang P, Liu S, Zhao S, Wang Y (2024) Structure-based discovery of a new type of scaffold compound as binding competitors for protein-bound Uremic Toxins. Sci Rep 14: 28152 doi: 10.1038/s41598-024-78766-9
4. Cunha RSD, Azevedo CAB, Falconi CA, Ruiz FF, Liabeuf S, Carneiro-Ramos MS, Stinghen AEM (2022) The Interplay between Uremic Toxins and Albumin, Membrane Transporters and Drug Interaction. Toxins (Basel) 14: 177 doi: 10.3390/toxins14030177
5. Meijers B, Zadora W, Lowenstein J (2024) A Historical Perspective on Uremia and Uremic Toxins. Toxins (Basel) 16: 227 doi: 10.3390/toxins16050227
6. Rosner MH, Reis T, Husain-Syed F, Vanholder R, Hutchison C, Stenvinkel P, Blankestijn PJ, Cozzolino M, Juillard L, Kashani K, Kaushik M, Kawanishi H, Massy Z, Sirich TL, Zuo L, Ronco C (2021) Classification of Uremic Toxins and Their Role in Kidney Failure. Clin J Am Soc Nephrol 16: 1918–1928 doi: 10.2215/CJN.02660221
7. Sugio S, Kashima A, Mochizuki S, Noda M, Kobayashi K (1999) Crystal structure of human serum albumin at 2.5 Å resolution. Protein Eng 12: 439–446 doi: 10.1093/protein/12.6.439
8. Dassault Systèmes BIOVIA (2020) Discovery Studio Visualizer, v3.5. San Diego: Dassault Systèmes
9. Ajmal MR, Zaidi N, Alam P, Nusrat S, Siddiqi MK, Badr G, Mahmoud MH, Khan RH (2017) Insight into the interaction of antitubercular and anticancer compound clofazimine with human serum albumin: spectroscopy and molecular modelling. J Biomol Struct Dyn 35: 46–57 doi: 10.1080/07391102.2015.1132258
10. Owoloye AJ, Ligali FC, Enejoh OA, Musa AZ, Aina O, Idowu ET, Oyebola KM (2022) Molecular docking, simulation and binding free energy analysis of small molecules as PfHT1 inhibitors. PLoS One 17: e0268269 doi: 10.1371/journal.pone.0268269
11. Li M, McAuley E, Zhang Y, Kong L, Yang F, Zhou Z, Wu X, Liang H (2014) Comparison of binding characterization of two antiviral drugs to human serum albumin. Chem Biol Drug Des 83: 576–582 doi: 10.1111/cbdd.12270
12. Shahabadi N, Hadidi S, Kalar ZM (2016) Biophysical studies on the interaction of platinum(II) complex containing antiviral drug ribavirin with human serum albumin. J Photochem Photobiol B 160: 376–382 doi: 10.1016/j.jphotobiol.2016.05.006
13. Niwa T (2013) Removal of protein-bound uraemic toxins by haemodialysis. Blood Purif 35(Suppl 2): 20–25 doi: 10.1159/000350843
14. Sakai T, Takadate A, Otagiri M (1995) Characterization of binding site of uremic toxins on human serum albumin. Biol Pharm Bull 18: 1755–1761 doi: 10.1248/bpb.18.1755
15. Rysz J, Franczyk B, Ławiński J, Olszewski R, Ciałkowska-Rysz A, Gluba-Brzózka A (2021) The Impact of CKD on Uremic Toxins and Gut Microbiota. Toxins (Basel) 13: 252 doi: 10.3390/toxins13040252
16. Jiang H, Wang X, Zhou W, Huang Z, Zhang W (2025) Gut microbiota dysbiosis in diabetic nephropathy: mechanisms and therapeutic targeting via the gut-kidney axis. Front Endocrinol (Lausanne) 16: 1661037 doi: 10.3389/fendo.2025.1661037
17. Pieniazek A, Bernasinska-Slomczewska J, Gwozdzinski L (2021) Uremic Toxins and Their Relation with Oxidative Stress Induced in Patients with CKD. Int J Mol Sci 22: 6196 doi: 10.3390/ijms22126196
18. Miao H, Zhang SJ, Wu X, Li P, Zhao YY (2025) Tryptophan metabolism as a target in gut microbiota, ageing and kidney disease. Int J Biol Sci 21: 4374–4387 doi: 10.7150/ijbs.115359
19. Ellis RJ, Small DM, Vesey DA, Johnson DW, Francis R, Vitetta L, Gobe GC, Morais C (2016) Indoxyl sulphate and kidney disease: Causes, consequences and interventions. Nephrology (Carlton) 21: 170–177 doi: 10.1111/nep.12580