Molecular docking of eleven snake venom peptides targeting human immunodeficiency virus capsid glycoprotein as inhibitors

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ABSTRACT

Background: Snake venoms are mainly composed of a mixture of proteins and peptides with antiviral activity against several viruses including HIV. Therefore, snake venoms represent a promising source for new antiviral drugs.
Aim: The study examines the toxin's capacity to disrupt the spike glycoprotein of HIV, the virus accountable for the HIV epidemic.
Methods: The active protein structure of HIV and snake toxins was derived from the protein RCSB-PDB. The interactions between this toxin and the spike protein were evaluated using molecular docking software/interface such as "*Cluspro 2*" and analyzers such as "*PyMOL*" and "*Ligplot*". The objective was to identify potential pharmacophores that could be used as a basis for future drug development.
Results: The latest study findings uncover fascinating affinities and interaction patterns between snake poisons and the HIV spike glycoprotein. We analyzed the consequences of these interactions and their capacity to impair viral entry and infection.
Conclusion: This work highlights a prospective approach for the advancement of antiviral treatments, utilizing nature's collection of toxins as a basis for pharmacophore-based medication exploration against viral infections.
Keywords: HIV, Spike glycoprotein, Snake toxins, Molecular docking, Pharmacophore.

Introduction

Snake venom can be considered as a potential source of natural proteins and peptides that can inhibit the growth and replication of various viruses which has been proved against dengue virus, measles virus, yellow fever virus, Sendai virus, and HIV (da Mata É *et al.,* 2017). Even the noncytotoxic portion of the snake venom was identified to be active against the measles virus, which inhibited the replication of virus inside the cells (Rivero *et al.,* 2011). As such various clinical active molecules that are approved for clinical practice were derived from snake venoms like *captopril, integrilin, aggrastat* to name a few (Mohamed Abd El-Aziz *et al.,* 2019). On the other hand, snake venom and its components exhibit antithrombotic, antiplatelet, antibacterial, antifungal, antiparasitic,

and anti-inflammatory properties. Additionally, they show potential as antiviral agents against various viral infections (Chérifi and Laraba-Djebari, 2021). Hence, snake venom can be considered as a potential source for drug discovery related to antivirals like anti-HIV/anti-AIDS molecules.

Since the first cases of HIV in humans were reported in 1981, (Sharp and Hahn, 2011) researchers have been looking for a cure or practical treatment. Novel compounds that can assist address issues associated to HIV growth and transmission have been successfully developed through several successful attempts; nonetheless, an all-encompassing cure or treatment for HIV has not yet been discovered. However, there is optimism for future discoveries due to ongoing study

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and scientific improvements in the medical field (Xu *et al.,* 2023).

It is common knowledge that the HIV pandemic has killed millions of people globally and significantly impacted global health. Since the start of the epidemic, 85.6 million people [65.0-113.0 million] have contracted the HIV virus, and 40.4 million [32.9–51.3 million] have lost their lives to the infection. At the end of 2022, 39.0 million [33.1–45.7 million] persons worldwide were HIV positive, and that number was steadily rising (WHO, 2023). With a 27.9% HIV prevalence rate, Eswatini is first on the list of nations with the highest rate, followed by Lesotho (23.6%) and Botswana (22.8%) (WHO, 2023). These figures demonstrate how urgently global efforts to prevent and treat HIV must continue. There are several kinds of medications that can be used to control HIV and slow down the disease's progression, but none of them have shown to be sufficiently successful to stop the virus's spread and guarantee its total eradication. Thus, it is imperative to create novel and more potent HIV preventive and treatment approaches using an unconventional approach and the most recent state-of-the-art research technologies, such as molecular docking and drug development (Baig *et al.,* 2015; Ferreira *et al.,* 2015).

The study findings from virtual screening and molecular docking were used to produce medications such as *indinavir, ritonavir, saquinavir, and raltegravir* (Baig *et al.,* 2015). In terms of HIV/AIDS management, which is preferred, Due to their remarkable improvements in patient outcomes, quality of life, and life expectancy, these medications have completely changed the way that HIV/AIDS is treated. But no one entry-inhibition molecule was created in this manner.

Therefore, the goal of the current research is to produce entrance inhibitors for HIV/AIDS management by utilizing cutting-edge molecular biology tools and unique drug development approaches. Because entry inhibitors target the initial stages of viral replication, their development is essential for the management of HIV/AIDS. By keeping the virus from penetrating host cells, these inhibitors hope to limit its capacity to proliferate and propagate. Through the application of cutting-edge molecular biology methods and new drug discovery strategies, scientists intend to find and create potent entry inhibitors that will supplement the current therapy choices for HIV/AIDS. This continuing study has enormous potential to advance the fight against this worldwide pandemic and significantly improve patient outcomes focusing on reshaping the anti-HIV activity of biotoxins, estimating the strength of viral entry inhibition into the healthy cells, and identifying the strongest toxin with possible entry inhibition.

Materials and Methods

Selection of target and ligand protein

The 3D confirmers of electron microscopic, NMR and crystallographic coordinates of the HIV capsid protein and snake venom proteins ($n = 11$) structures were obtained from the protein data bank (Berman *et al.,* 2000; Goodsell *et al.,* 2015) with the following attributes: HIV capsid protein PDB IDs: 6ES8 (resolution: 1.90 Å) (Mallery *et al.,* 2018), *Bothrops asper venom* 1: PDB ID: 5TFV (resolution: 2.54 Å) (Salvador *et al.,* 2017), *Bothrops jararaca venom* 2: PDB ID: 3DSL (resolution: 2.70 Å) (Muniz *et al.,* 2008), *Russell's viper* venom 3: PDB ID: 3S9B (resolution: 1.90 Å) (Nakayama *et al.,* 2011), *Bothrops jararacussu venom* 4: PDB ID: 4E0V (resolution 3.10Å) (Ullah *et al.,* 2012), Protobothrops flavoviridis *venom* 5: PDB ID: 1WVR (Calcium Channel Blocker) (resolution 2.40 Å) (Shikamoto *et al.,* 2005), Crotalus durissus terrificus *venom* 6: PDB ID: 1UOS (Convulxin) (resolution 2.70 Å) (Batuwangala *et al.,* 2004), Deinagkistrodon acutus *venom* 7: PDB ID: 3UBU (platelet inhibitor) (resolution 1.91 Å) (Gao *et al.,* 2012), Echis carinatus *venom* 8: PDB ID: 1RMR (disintegrin) (resolution 2.50 Å) (Bilgrami *et al.,* 2004), Gloydius blomhoffii *venom* 9: PDB ID: 4AA2 (resolution 1.99 Å) (Akif *et al.,* 2012), Pseudonaja textilis *venom* 10: PDB ID: 3BYB (protease inhibitor) (resolution 1.63 Å) (Millers *et al.,* 2009), and C. durissus *venom* 11: PDB ID: 4GV5 (cell penetrating peptide) (resolution 1.70 Å) (Coronado *et al.,* 2013).

In order to make the protein and ligand proteins deemed filtered for further processing, the water molecules that were present in the structure were removed, along with the ligands and hetatms. Polar hydrogens were then added as needed.

A drug candidate for each ligand was assessed using Lipinski's rule of five. Molecular weight less than 500 Da, a maximum of 5 H-bond donors, 10 hydrogen bond acceptors, and a maximum of 5 *logP* (octanol-water distribution) factors.

Protein–protein interactions: Cluspro2

*Cluspro2 (*https://cluspro.bu.edu/login.php*)* (Kozakov *et al.,* 2017; Vajda *et al.,* 2017) which utilizes an automated approach, was recommended for protein–protein docking. The *cluspro2* server received the *pdb* files of the spike protein and several ligand proteins. *Balanced cluster scores, hydrophobic preferred cluster scores, electrostatic cluster scores, Vander walls, and electrostatic cluster scores* were the outcomes of the automated protein-protein docking. The maximum negative score was regarded as the lowest score because the data was expressed in negative values. *Pymol (*https://pymol.org/2/*) and ligplot plus v2.2 (*https://www.ebi.ac.uk/thornton-srv/software/LigPlus/download.html*)* (Laskowski and Swindells, 2011) were used to analyze the molecularly interacted models. The results showed the length of hydrogen bonds and interactive amino acids in the two proteins' interactive regions. The following tables and figures present the study's findings.

Ethical approval

Not needed for this study.

Results

Molecular docking experiments were carried out to examine eleven possible poisons of species that are members of the Viperidae, Elapidae, and Atractaspididae families. Each of these compounds was docked against the target protein and ranked based on its dock score (Table 1).

The condensed findings of molecular docking studies showed robust connections in different protein-protein interactions with a particular binding affinity (docking scores) between 11 potential ligands (toxins) and the HIV surface glycoprotein. The docked model with the lowest binding energy and maximum binding affinity indicated the most stable interaction between the ligand/protein and the target protein. The ligands were selected on the basis of their binding affinities. *PyMOL* (for protein-protein interaction) was used to visualize structures with high dock scores (Yuan *et al.,* 2017) and *Ligplot* was preferred to visualize the interactions among the amino acids. (Laskowski and Swindells, 2011) The individual amino acids involved in protein-protein binding were revealed by the details of hydrophobic and hydrogen bond interactions. Single chains: To conduct the docking and obtain findings that may interact with protein toxins, a single chain of the HIV spike protein was used (Table 1).

Details of HIV spike protein, and its interactions with various toxins of snake species of Elapidae, Viperidae families (PyMOL derived)

HIV Surface-glycoprotein–toxin 1 (*B. asper*) complex: molecular interactions with best wander wall's forces scores

The HIV-surface-glycoprotein- *B. asper* toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −300.1, −993.4, −1150.8, and −900.5. As a result of this proteins interact with hydrogen bonds between LYS 132 B of *B. asper* toxin and the ASN 121 A of HIV-surface-glycoprotein with the shortest distance of 2.6 Å. (Fig. 1) (Table 1).

HIV Surface-glycoprotein–toxin 2 (B. jararaca) complex molecular interactions with best-balanced cluster scores

The HIV-surface-glycoprotein- *B. jararaca* toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −243.7, −1281.9, −1597, and −1312.6. As a result of this proteins interact with hydrogen bonds between TYR 387 B of *B. jararaca* toxin and ASN 389 A of HIV-surface-glycoprotein with the shortest distance of 2.7 Å. (Fig. 2) (Table 1).

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 3 (PDB ID 3S9B)
HIV Surface-glycoprotein–toxin 3 (Russell's viper) complex

The HIV-surface-glycoprotein- *Russell's viper* toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −219.4, −1112.2, −1325.6, and −1056.9. As a result of this proteins interaction with hydrogen bonds between ARG 107 B of *Russell's viper toxin* and ALA 209 A of HIV-surface-glycoprotein with the shortest distance of 2.71 Å. (Fig. 3) (Table 1).

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 4 (PDB ID 4E0V)
HIV Surface-glycoprotein–toxin 4 (*B. jararacussu*) complex

The HIV-surface-glycoprotein- *B. jararacussu* toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −251.9, −1049, −1167.7, and −1009.3. As a result of this proteins interaction with hydrogen bonds between LYS 191 B of *B. jararacussu toxin* and TYR 436 A of HIV-surface-glycoprotein with the shortest distance of 2.7 Å. (Fig. 4) (Table 1).

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 5 (PDB ID 1WVR)
HIV Surface-glycoprotein–toxin 5 (*P. flavoviridis*) complex

The HIV-surface-glycoprotein- P. flavoviridis toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −207.9, −951.2, −1239.9, and −919.3. As a result of this proteins interaction with hydrogen bonds between PRO 171 B of P. flavoviridis *toxin* and GLY 208 A of HIV-surface-glycoprotein with the shortest distance of 2.6 Å (Fig. 5) (Table 1).

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 6 (PDB ID 1UOS)
HIV Surface-glycoprotein–toxin 6 (C. durissus terrificus) complex

The HIV-surface-glycoprotein- C. durissus terrificus toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −222.7, −1151.9, −1299, and −1037.8. As a result of this proteins interaction with hydrogen bonds between GLU 94 B of C. durissus terrificus *toxin* and VAL 116 A of HIV-surface-glycoprotein with the shortest distance of 2.5 Å (Fig. 6) (Table 1).

Table 1. Protein-protein docking results of 'Cluspro2', analysed through *PyMOL*, visualised through *Ligplot*: HIV capsid protein (PDB ID: 6ES8) as target and several biotoxins as ligand-proteins for the docking analysis.

Sr No And Name	PDB ID	RMSD	Hydrogen bond interactions (Å units)	Amino acids (in the reacted pocket) of ligand protein	Vander walls & electrostatic force cluster scores	Electrostatic favoured— cluster scores	Hydrophobic favoured— cluster scores	Balanced score— cluster scores
1. *Bothrops asper venom*	5TFV	6.821	2.6–3.0	LYS 132 B—ASN 121 A (Details are provided in Annexure I)	−300.1	−993.4	−1,150.8	−900.5
2. *Bothrops jararaca venom*	3DSL	16.096	2.7–3.0	TYR 387 B—ASN 389 A (Details are provided in Annexure II)	−243.7	−1,281.9	−1,597	−1312.6
3. *Russell's viper venom*	3S9B	16.177	2.71–2.74	ARG 107 B—ALA 209 A (Details are provided in Annexure III)	−219.4	−1,112.2	−1,325.6	−1056.9
4. *Bothrops jararacussu venom*	4E0V	18.977	2.7–3.2	LYS 191 B—TYR 436 A (Details are provided in Annexure V)	−251.9	−1,049	−1,167.7	−1,009.3
5. *Protobothrops flavoviridis venom*	1WVR	5.374	2.6–3.2	GLY 208 A—PRO 171 B (Details are provided in Annexure VI)	−207.9	−951.2	−1,239.9	−919.3
6. *Crotalus durissus terrificus venom*	1UOS	21.810	2.5–3.2	VAL 116 A—GLU 94 B SER 90 C—SER 90 A TYR 91 A—GLU 47 D (Details are provided in Annexure VII)	−222.7	−1,151.9	−1,299	−1,037.8
7. *Deinagkistrodon acutus venom*	3UBU	8.903	2.5–3.3	THR 95 B—ASN 116 A (Details are provided in Annexure VIII)	−244.1	−976.2	−1,320.9	−974.3
8. *Echis carinatus venom*	1RMR	4.805	2.6–3.1	THR 188 A—PRO 9 B (Details are provided in Annexure IX)	−188.7	−1,030.3	−1,421.9	−1015.5
9. *Gloydius blomhoffii venom*	4AA2	15.027	2.5–3.0	TYR 507 A—ILE 9 P (Details are provided in Annexure X)	−228.4	−917.3	−988.6	−840.1

(Continued)

Sr No And Name	PDB ID	RMSD	Hydrogen bond interactions (Å units)	Amino acids (in the reacted pocket) of ligand protein	Vander walls & electrostatic force cluster scores	Electrostatic favoured—cluster scores	Hydrophobic favoured—cluster scores	Balanced score—cluster scores
10. Pseudonaja textilis textilis *venom*	3BYB	5.084	2.5–3.1	ARG19 A—GLY 42 B LYS 50 A—ASP 28 C (Details are provided in Annexure XI)	−254.9	−1,287.1	−1,611.2	−1,226.1
11. Crotalus durissus terrificus *venom*	4GV5	1.558	2.4–3.1	LYS 35 A—GLU 15 B ARG 31 A—GLY 40 C (Details are provided in Annexure XII)	−217.5	−1,115	−1,501.7	−217.5

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 7 (PDB ID 3UBU)
HIV Surface-glycoprotein–toxin 7 (D. acutus) complex
The HIV-surface-glycoprotein- D. acutus toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favoured—Cluster scores, Balanced score—Cluster scores are −244.1, −976.2, −1320.9, and −974.3. As a result of this proteins interaction with hydrogen bonds between THR 95 B of D. acutus *toxin* and ASN 116 A of HIV-surface-glycoprotein with the shortest distance of 2.5 Å (Fig. 7) (Table 1).

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 8 (PDB ID 1RMR)
HIV Surface-glycoprotein–toxin 7 (E. carinatus) complex
The HIV-surface-glycoprotein- E. carinatus toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favoured—Cluster scores, Balanced score—Cluster scores are −188.7, −1030.3, −1421.9, and −1015.5. As a result of this proteins interaction with hydrogen bonds between PRO 9 B of E. carinatus *toxin* and THR 188 A of HIV-surface-glycoprotein with the shortest distance of 2.6 Å (Fig. 8) (Table 1).

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 9 (PDB ID 4AA2)
HIV Surface-glycoprotein–toxin 7 (G. blomhoffii) complex
The HIV-surface-glycoprotein- G. blomhoffii toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −228.4, −917.3, −988.6, and −840.1. As a result of this proteins interact with hydrogen bonds between ILE 9 P of G. blomhoffii *toxin* and TYR 507 A of HIV-surface-glycoprotein with the shortest distance of 2.5 Å (Fig. 9) (Table 1).

HIV Surface-glycoprotein–toxin 7 (P. textilis) complex with best electrostatic favored—cluster scores & hydrophobic favored—cluster scores
The HIV-surface-glycoprotein- *P. textilis* toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −228.4, −917.3, −988.6, and −840.1. As a result of this proteins interaction with hydrogen bonds between GLY 42 B and ASP 28 C of *P. textilis toxin* and ARG19 A and LYS 50 A of HIV-surface-glycoprotein with the shortest distance of 2.5 Å (Fig. 10) (Table 1).
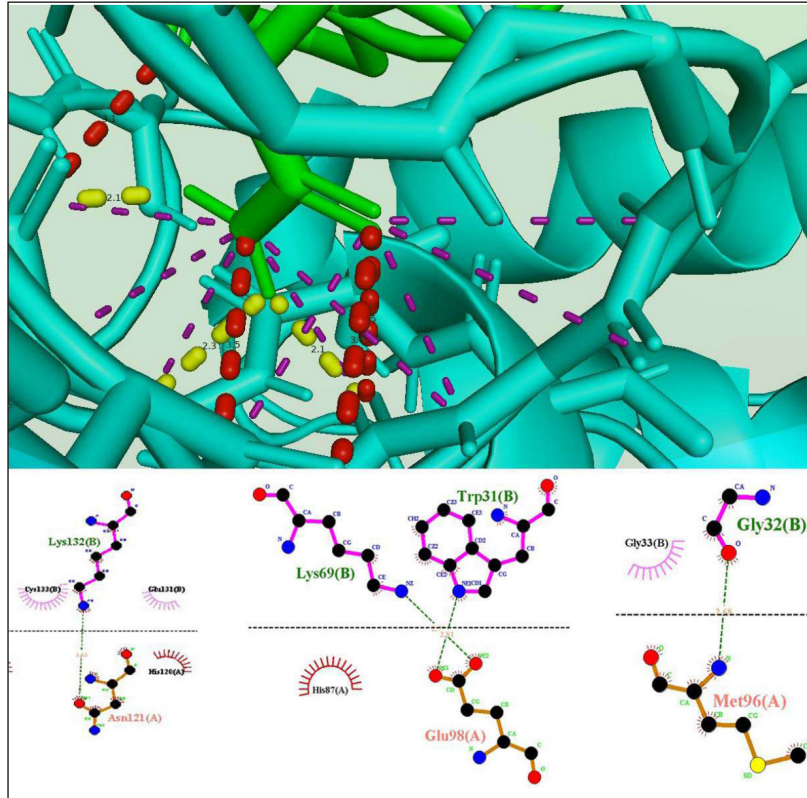
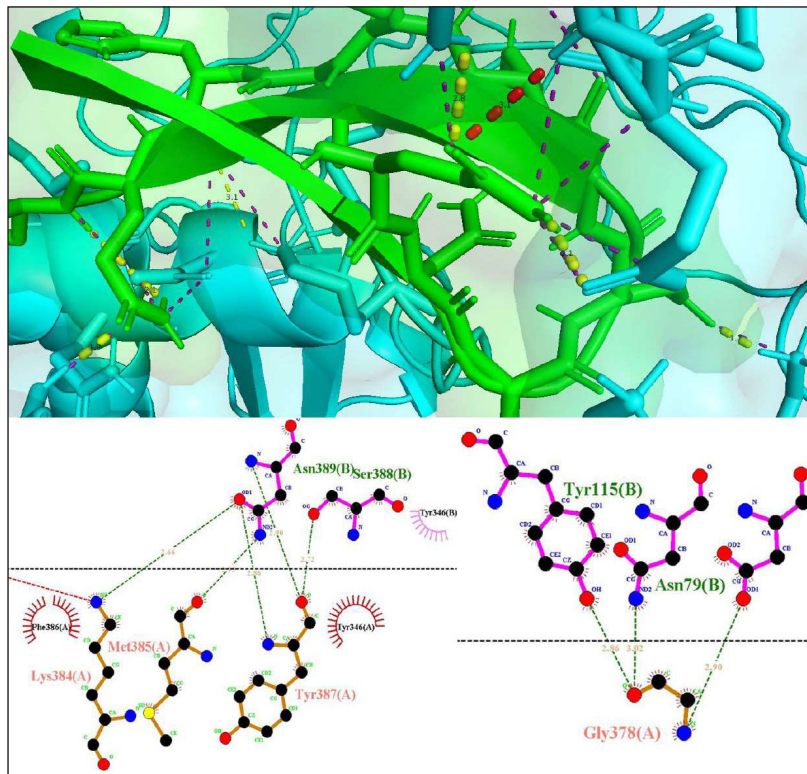**Fig. 1.** HIV surface glycoprotein interaction with *B. asper* B.

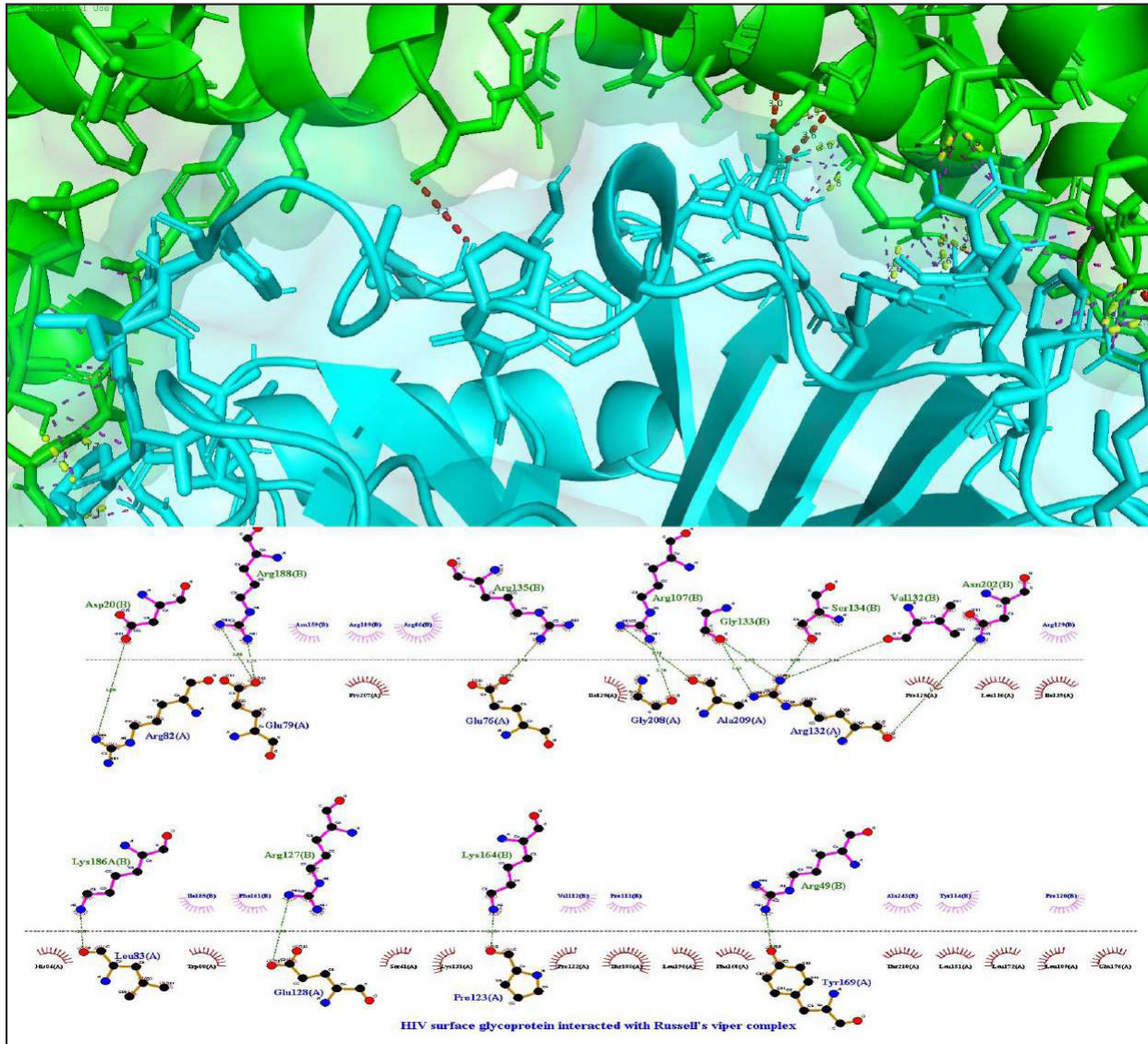**Fig. 2.** HIV surface glycoprotein interaction with *B. jararaca* B.

Fig. 3. HIV surface glycoprotein with Ryssell's viper.

Details of interaction between HIV Surface-glycoprotein (PDB ID 6ES8) with toxin 11 (PDB ID 4GV5)

HIV Surface-glycoprotein–toxin 7 (C. durissus terrificus) complex

The HIV-surface-glycoprotein- C. durissus terrificus toxin complex docked with significant binding affinities of Vander walls & Electrostatic force Cluster scores, Electrostatic favored—Cluster scores, Hydrophobic favored—Cluster scores, Balanced score—Cluster scores are −217.5, −1115, −1501.7, and −217.5. As a result of this proteins interaction with hydrogen bonds between GLU 15 B of C. durissus terrificus *toxin* and LYS 35 A of HIV-surface-glycoprotein with the shortest distance of 2.4 Å (Fig. 11) (Table 1).

Discussion

Strengthening human responses against the HIV virus is essential to ensuring human sustainability. A significant number of researchers globally are working on the development of new molecules or rethinking old ones in an attempt to control and slow the spread of HIV (Piscaglia *et al.,* 2021). Parallelly, the present study aims to discover a new medication that might safeguard lives by analyzing the effects of snake poisons from the *Elapidae and Viperidae* families on the HIV surface spike protein. (Siniavin *et al.,* 2022) Following a comprehensive analysis of the literature, eleven toxins from snakes in the *Elapidae and Viperidae* families were selected, as indicated in Table 1, and the HIV surface spike protein of the capsid with PDB ID: 6ES8 was selected for testing. Every toxin protein
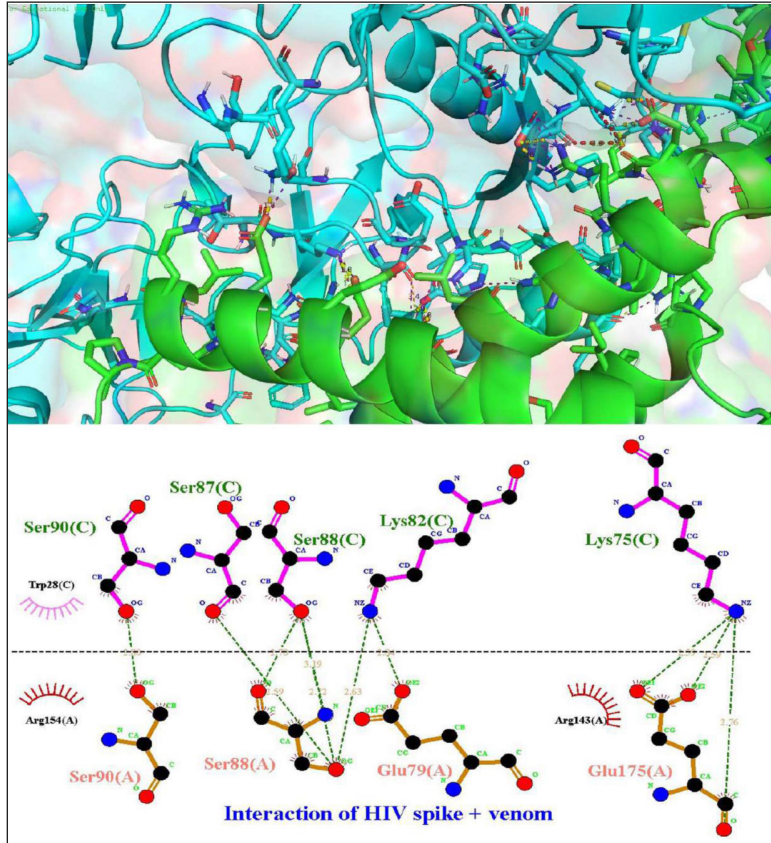
Fig. 4. HIV surface glycoprotein interaction with *B. jararacussu* ligplotv.

Fig. 5. HIV surface glycoprotein interaction with *P. flavoviridis* ligplot.

Fig. 6. HIV surface glycoprotein interaction with *C. durissus* ligplot.
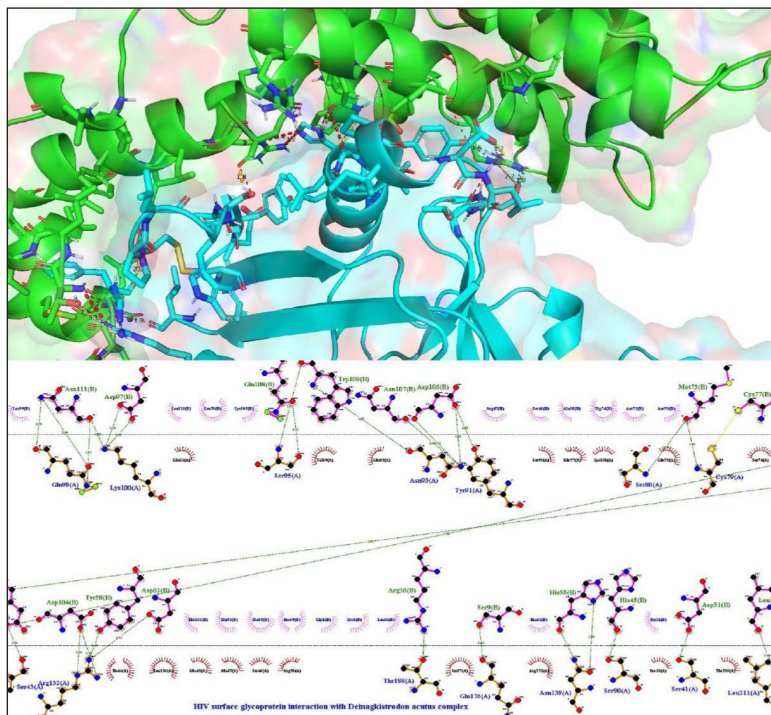

Fig. 7. HIV surface glycoprotein interactions with Deinagkistrodon cutus complex ligplot.
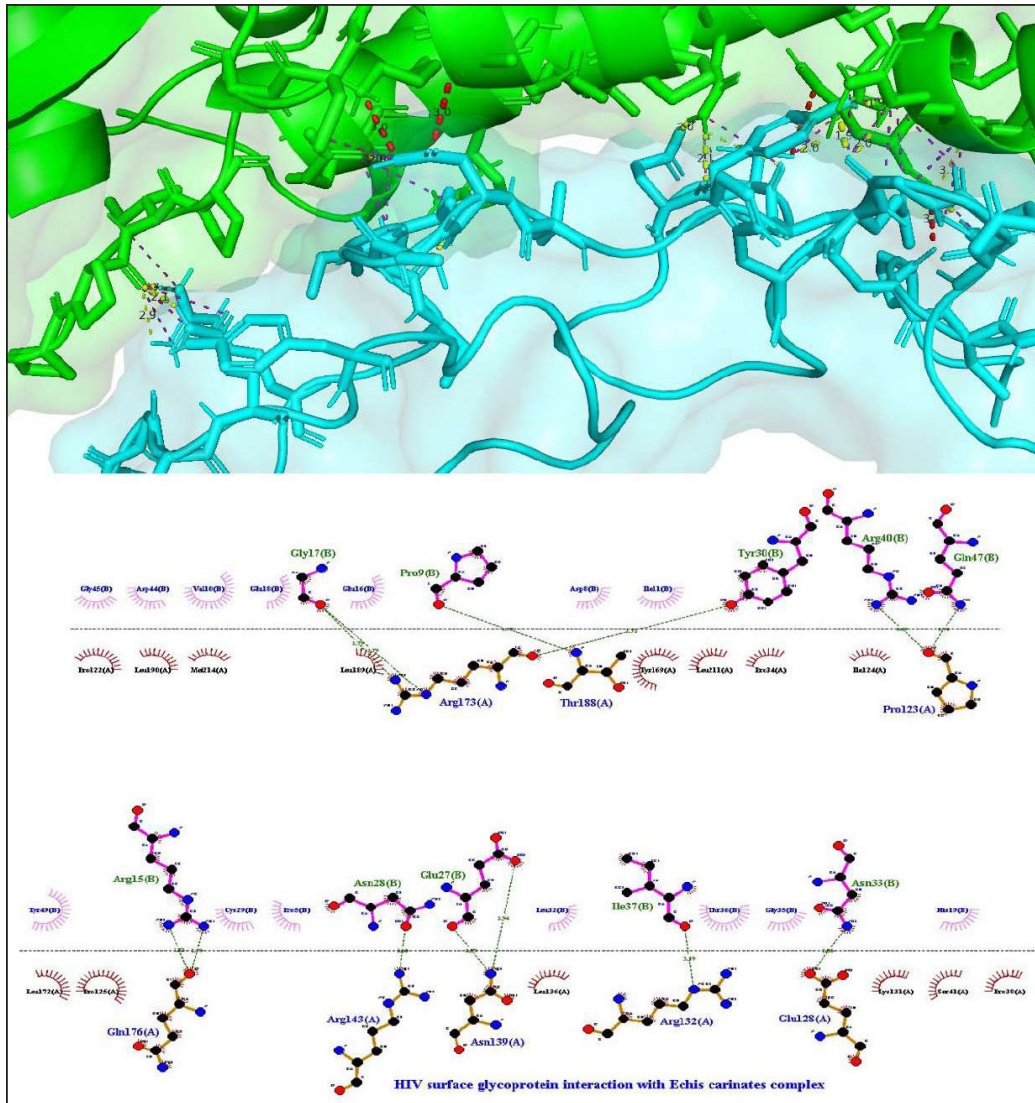
Fig. 8. HIV surface glycoprotein interaciton with *E. carinatus* ligplot.

was selected to undergo processing using *cluspro-2*, (Kozakov *et al.,* 2017) followed by an automated approach and *PyMOL* analysis and visualization.

The protein—protein interaction of all the toxins was the least for Hydrophobic favored—Cluster scores of −1611.2 were noted for the *P. textilis* toxin and the highest score was noted for G. blomhoffii −988.6. The lowest Electrostatic favored—Cluster scores of -1287.1 was noted for the *P. textilis* toxin and the highest score was noted for G. blomhoffii −917.3. The lowest Vander walls & Electrostatic force—Cluster scores of −300.1 was noted for the *B. asper* and the highest with −188.7was noted for E. carinatus and the lowest Balanced score—Cluster scores of −1312.6 was noted for the *Bothrops jararaca* and the highest with −840.1 was noted for G. blomhoffii. The Crotalus durissus terrificus toxin interacted with the target protein at

a competitive H-bond distance of 2.4 Å. The above-given scores prove the fact that snake venom could be a good source of developing a drug which is helpful in the treatment of chronic and challenging disorders and infections like HIV (Meenakshisundaram *et al.,* 2009; Uzair *et al.,* 2018).

It is evident that the *P. textilis* toxin is a protease inhibitor named Textilinin-1, a Kunitz-type serine protease inhibitor including plasmin and trypsin. (Millers *et al.,* 2009) Which was obtained from the Australian common brown snake venom was expressed with good docking scores and stood up as the most potent candidate for the new drug research and development as anti-HIV. Redesigning the protein in a favorable way may prove beneficial in limiting the spread of viral infections like HIV. An extensive literature review revealed that a few noticeable manuscripts are available reflecting
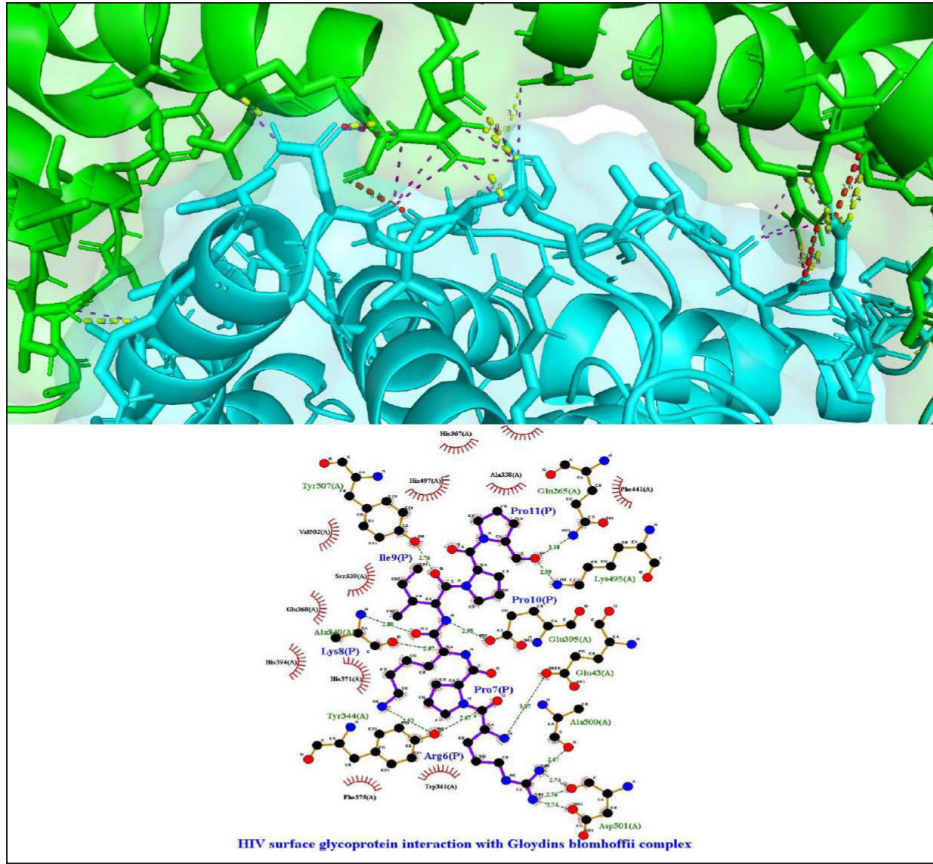
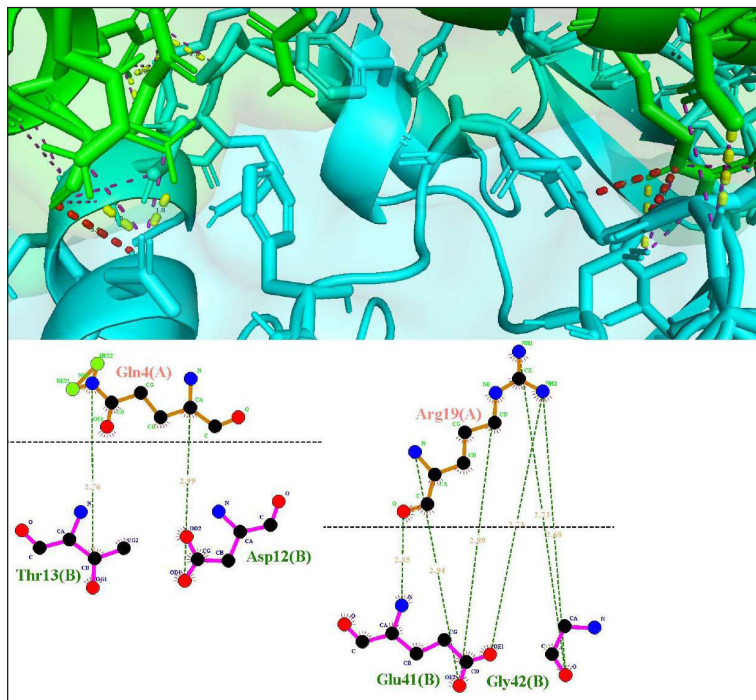**Fig. 9.** HIV surface glycoprotein interaction with *G. blomhoffii* complex ligplot.

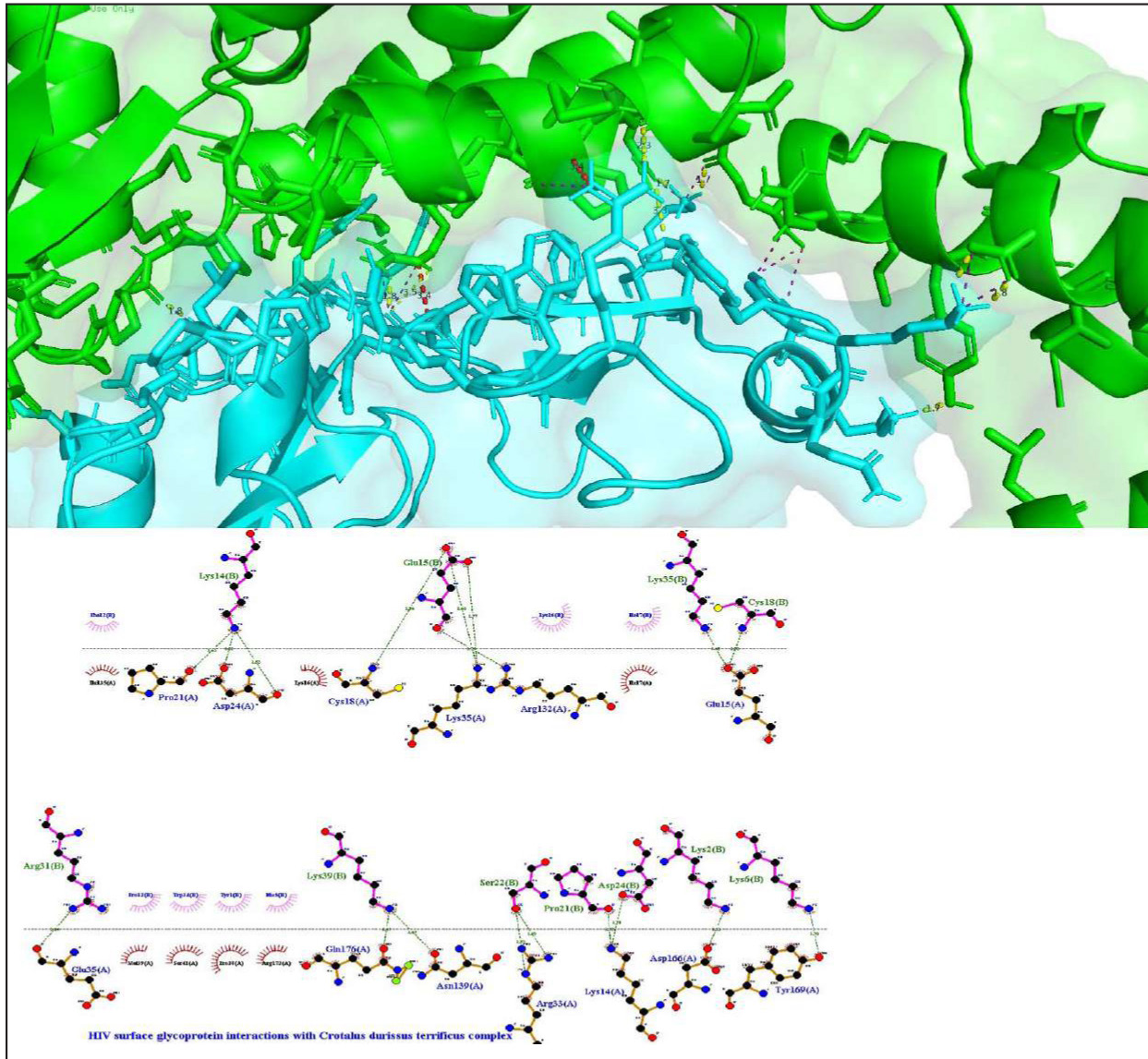**Fig. 10.** HIV surface glycoprotein interaction with *P. textilis* textilis B.

Fig. 11. HIV surface glycoprotein interaction with *C. durissus* complex ligplot.

the need of the current research, (Neri *et al.,* 1990; Khusro *et al.,* 2018; Oliveira *et al.,* 2022); however, not concentrating on the toxins but on other antivirals, agent to improve and prepare the molecule with greater affinity (Alrajhi Abdulrahman and Almohaizeie, 2008). Hence, the current study is highly justifiable in this scenario. Interferons are one the desired candidates being proteinaceous in origin is highly applicable in the management of viral infections including HIV and this garners a chance for the molecules of the current investigation eleven of which are toxins but proteins to be a reliable source as anti-HIV in future. (Alrajhi Abdulrahman and Almohaizeie, 2008)

Furthermore, the lowest Vander walls & Electrostatic force—Cluster scores of −300.1 was noted for the *B. asper* and the lowest Balanced score—Cluster scores of −1312.6 was noted for the *B. jararaca* which can act as potential candidates for the novel drug development and research for preventing the vial entry into a healthy cell, like other entry inhibitors (Lobritz *et al.,* 2010). Remodeling the amino acid sequence of the human cellular structures may result in the redesigning of the entry point of the for the virus into humans which may also can prevent the entry of the virus in healthy individuals (German Advisory Committee Blood 2016; Gutiérrez-Sevilla *et al.,* 2021).

Conclusion

Snake venom can be a potential therapeutic source of anti-HIV/antiviral candidates that could potentially

treat or reduce the incidences of HIV with acceptable to least side effects. 11 potential animal toxins from various families of snakes' species were molecularly docked and revealed several binding interactions with the target protein. *Pseudonaja textilis* toxin a protease inhibitor named Textilinin-1, a Kunitz-type serine protease inhibitor including plasmin and trypsin exhibited favourable interactions with HIV capsid-glycoprotein with the highest affinities. These peptides could be used as HIV capsid-glycoprotein inhibitors because, according to molecular docking studies, they can prevent the interaction between human cells and the HIV capsid-glycoprotein which could be supported by the high-throughput screenings, cell line studies, preclinical studies, and human trials to concrete the evidence. Nonetheless, this research could be considered as the beginning of the new search for an anti-HIV entry inhibitor.

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