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Identification of novel antagonists of the ecdysone receptor from the desert locust (*Schistocerca gregaria*) by *in silico* modelling

S. A. Hemmati*

***Corresponding Author:** Assistant Professor, Department of Plant Protection, Faculty of Agriculture, Shahid Chamran University of Ahvaz, Ahvaz, Iran (sa.hemmati@scu.ac.ir)

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Abstract

The desert locust, *Schistocerca gregaria* Forsskål, is the most destructive migratory pest, which continually damages large areas of cropland and pastures in various parts of the world. Chemical insecticides are currently being used to control desert locusts. However, due to the harmful effects of conventional insecticides on human health and the environment, as well as the emergence of insecticides-resistant insects, alternative pest management programs must be developed. Given the critical role of the ecdysone receptor (EcR) in insect development, this study aimed to use computational tools to identify compounds with antagonistic properties against the desert locust EcR. Understanding the biochemical and structural properties of EcR is required for designing target-specific inhibitors, so we first used several bioinformatics tools to investigate the physicochemical properties, secondary structures, and topology of EcR from *S. gregaria*. SWISS-MODEL was used to predict the three-dimensional structural models of EcR, and the reliability of the predicted model was validated by various programs. Molecular docking studies between eight locust-derived protease inhibitors and the predicted model of EcR revealed the antagonistic capacity of all the studied inhibitors against EcR. However, the inhibitor 1KJ0 had the best docking score, the lowest binding energy and dissociation constant, and the greatest number of hydrogen bonds and non-bonded contacts with EcR, indicating its strong antagonistic potency against EcR. Our findings highlight the importance of computational studies in identifying novel antagonists to a target protein. However, *in vitro* and *in vivo* investigations are further required to validate the potency of the introduced compound.

Keywords: Schistocerca gregaria, locust protease inhibitors, molecular docking, pest management

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Introduction

The desert locust (*Schistocerca gregaria* Forsskål) is widely regarded as the world's most destructive migratory pest (Symmons & Cressman, 2001). Locusts exhibit two distinct behavioral states known as solitarious and gregarious (Simpson & Sword, 2008). Locusts live in isolation as cryptic sedentary individuals during the solitarious phase (Cullen et al., 2017). However, once they enter the gregarious phase, they form dense swarms that migrate long distances and voraciously consume any green vegetation in their path, causing substantial damages to pastures and crops (Kennedy, 1951; Le Gall et al., 2019). Desert locusts have been reported to severely affect thousands of hectares of land in Iran, primarily in the southern provinces, threatening food security and rural livelihoods (OCHA, 2020; OHCA, 2020).

The most common management strategy for protecting plants against desert locusts and increasing crop yields is aerial and ground spraying of chemical insecticides (Dobson, 2001). Despite the benefits of chemical insecticides, overreliance on these compounds results in the emergence of resistant insects (Peshin & Dhawan, 2009). Furthermore, insecticides may adversely affect the environment, ecosystems, and human health (Hassaan & El Nemr, 2020). As a result, additional research is required to develop effective pest management tools with high target specificity and low environmental impact for desert control.

Insect growth regulators (IGRs) are considered as attractive alternatives to conventional insecticides. IGRs are compounds that mimic the action of insect hormones and thereby interfere with the growth and development processes of insects (Subramanian & Shankarganesh, 2016). IGRs are known to be highly selective against target pests and are less harmful to human health and the environment (Wright, 1976). Ecdysteroids are steroid hormones that regulate many physiological processes in insects (Koolman 1989). 20-Hydroxyecdysone (20E), the active form of ecdysone, binds to its cognate nuclear receptor and triggers signaling cascade, which ultimately initiates molting and metamorphosis processes in insects (Fahrbach et al., 2012; Nakagawa & Henrich, 2009). Given that 20E regulates key physiological processes in insects, IGRs that interfere with 20E signaling pathway could be considered ideal alternatives for the sustainable management of insecticide-resistant pests.

Ecdysteroid-mimicking compounds interfere with insect development through binding to the ecdysteroid receptor (Hu et al., 2018). The functional receptor is a heterodimer composed of two proteins: the ecdysone receptor (EcR) and the ultraspiracle protein (USP) (Yao et al., 1993). The interaction of the receptor with 20E is mediated through the ligand binding domain (LBD) of EcR (Ekoka et al., 2021). Ecdysone antagonists compete with 20E for binding to EcR, inhibiting the signaling cascade required for molting and metamorphosis and causing developmental arrest in larvae (Muema et al., 2017). Ecdysone antagonists have not been used effectively for pest management, and therefore, there is an opportunity to discover novel compounds with antagonistic activities against EcR to reduce the devastating impact of desert locusts on crop and livestock production.

Developing a new pesticide is a time-consuming and costly process (McDougall, 2016). On the other hand, using computational approaches (i.e., *in silico* tools) helps reduce the costs and time associated with the initial stages of the discovery process (Kuhr and Motoyama 1998). Computational methods enable us to make reliable predictions about ligand-target interactions, identify inhibitor binding sites on the target molecule, analyze the physicochemical properties of the binding site and estimate ligand-target affinities (Lin et al., 2020). After discovering promising candidates via computational analyses, *in vitro* experiments can be carried out to evaluate the efficacy of selected molecules.

Considering the functional importance of EcR in the growth and development of insects, we first employed bioinformatics tools to predict the 3D structure model of the receptor protein. Then, the publicly available structures of eight locust-derived protease inhibitors from desert locusts (*S. gregaria*) and migratory locusts (*Locusta migratoria*) were used to perform molecular

docking simulations to predict the interaction of locust-derived inhibitors with EcR in order to screen for compounds with high binding affinity scores. The *in silico* approach adopted in this study enabled the discovery of novel candidates with potential antagonistic activities against EcR. However, experimental investigations are further required to validate the accuracy of the adopted methodology in predicting the interaction of proposed candidates with EcR.

Materials and Methods

Data retrieval and *in silico* physicochemical characterization

Amino acid sequence of the desert locust EcR (accession number: A0A109P395) was obtained from the Uniprot (universal protein resource) database (www.uniprot.org/). Expasy ProtParam was used to characterize physicochemical properties of EcR, including molecular weight, theoretical pI (isoelectric point), instability index, and aliphatic index (https://web.expasy.org/protparam/) (Gasteiger et al., 2005). The secondary structure of EcR was predicted by SOPMA (self-optimized prediction method with alignment) (http://npsa-pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=npsa_sopma.html) (Geourjon & Deléage, 1995).

Transmembrane helices for the protein were predicted using the TMHMM (Transmembrane Helices; Hidden Markov Model) Server (http://www.cbs.dtu.dk/services/TMHMM) (Krogh et al., 2001). The amino acid composition of the binding site of EcR was identified by the CASTp (computed atlas for surface topography of proteins) server (http://sts.bioe.uic.edu/castp/) (Tian et al., 2018). Furthermore, the current study focused on the insects' inhibitors, whose structures were determined using the X-ray crystallography method, and consequently 3D (three-dimensional) structures of eight locust-derived protease inhibitors were retrieved from the PDB (the protein data bank) archive (https://www.rcsb.org/).

3D structure modelling and quality assessment

The 3D structure model of the desert locust EcR was generated using SWISS-MODEL, which is an automated protein structure homology modelling server (Schwede, 2003). Briefly, the amino acid sequence of desert locust EcR was searched against a library of proteins with experimentally determined structures to identify suitable templates. A set of 50 top-ranked templates were selected from the SWISS-MODEL template library (SMTL) based on a score combining sequence coverage and sequence identities and sorted according to the GMQE score. GMQE is a quality estimate of the expected accuracy of generated models by combining properties from the target–template alignment and the template structure.

3D structural models were built based on top-ranked templates and the accuracy of the generated models was evaluated using the QMEAN (qualitative model energy analysis) function, which predicts the global and local quality estimates on the basis of a single model (Benkert et al., 2008). QMEAN describes the major geometrical aspects of protein structures including torsion angle potentials (local geometry), a secondary structure-specific residue-based statistical potential (long-range interactions), a solvation potential for the burial of residues as well as the agreement between the predicted and calculated secondary structure and solvent accessibility (Benkert et al., 2008). The QMEAN global score was transformed into a Z-score, which was calculated by relating the QMEAN score of the query model to the scores of experimentally determined structures of similar size. The overall quality of the models was predicted based on GMQE and QMEANDisCo (QMEAN - distance constraints) global scores. QMEANDisCo global score is the average per-residue QMEANDisCo score, which adds distance constraint to QMEAN measurements (Studer et al., 2020).

The quality of models was further evaluated using structural analysis and verification server (SAVES) tools, including PROCHECK, ERRAT, and VERIFY 3D. The stereochemical quality of the model was evaluated by PROCHECK through Ramachandran plot analysis (Laskowski et al., 1993), and the distribution of non-bonded interactions between different types of atoms in the model was assessed by ERRAT (Colovos & Yeates, 1993). VERIFY3D was used to determine the

compatibility of the 3D model with its amino acid sequence (1D) (Bowie et al., 1991). Additionally, the potential errors in the 3D model were determined by the ProSA (Protein Structure Analysis) server, which produces a Z-score indicating the overall quality of the model (Wiederstein & Sippl, 2007). Template selection, alignment of target sequence and template structure(s), 3D modeling, and model quality evaluation were repeated until a satisfactory model was achieved.

Docking Simulations

The interactions between the eight locust-derived protease inhibitors and the key residues of EcR were investigated using the HADDOCK (High Ambiguity Driven biomolecular DOCKing) web server (de Vries et al., 2010). Docking was performed with default parameter settings. Two types of ambiguous interaction restraints (AIRs) derived from experimental data were defined to guide the docking process: (1) solvent-accessible residues at the predicted interaction interface as active residues and (2) solvent-accessible surface residues within 6.5 Å from any active residue as passive residues.

The first docking step (i.e., the rigid body energy minimization step) generated 1000 models. The top 200 complexes were clustered based on RMSD (root mean square deviation) and ranked by average HADDOCK scores within each cluster. In the final step, refinement of selected structures was performed using energy minimization. Additionally, PRODIGY (protein binding energy prediction) webserver (https://bianca.science.uu.nl/prodigy/) was used to calculate the binding energy (ΔG) and dissociation constant (K_d) at 25°C, as indicators of the binding affinity of locust-derived protease inhibitors to EcR. Hydrogen bonds and non-bonded contacts between the protease inhibitor and EcR were calculated and displayed by the PDBsum server (de Beer et al., 2014). Molecular structures were visualized using the UCSF Chimera package version 1.14 (Pettersen et al., 2004)

Results and Discussion

Physicochemical characterization of EcR

Expasy Protparam tool computes various physical and chemical properties of a protein from its amino acid sequence. Table 1 summarizes the predicted properties of the desert locust EcR by Expasy Protparam. Our analysis revealed that EcR was an alkaline protein (pI value of 8.23) with a molecular weight of ~58 kDa. Furthermore, an instability index higher than 40 was calculated for EcR, suggesting that the protein is potentially unstable under *in vitro* conditions. Additionally, the relatively high aliphatic index calculated for EcR (75.47) was indicative of the thermostability of the protein over a wide range of temperatures. Finally, the predicted negative GRAVY value (–0.394) for EcR suggested that the protein is more likely to be hydrophilic (i.e., water-soluble).

Prediction of secondary structures and transmembrane helices

SOPMA is commonly used to predict the secondary structures of a protein from its amino acid sequence (Geourjon & Deléage, 1995). Secondary structure analysis by SOPMA revealed that random coils (46.99%) and α-helices (36.28%) were the predominant structural elements present in EcR, as opposed to β-strands (10.71%) and β-turns (6.02%) that occurred less frequently in the protein.

TMHMM predicts membrane the presence of transmembrane helices in the proteins based on a hidden Markov model (Krogh et al., 2001). Prediction of the presence of transmembrane helices suggests the protein of interest is embedded in the membrane, whereas the absence of transmembrane helices means the protein is not membrane-associated. In this study, no transmembrane helices were predicted in EcR using TMHMM, suggesting the localization of this protein in the cytoplasm or nucleus.

Determination of the binding site

Locust-derived protease inhibitors are required to specifically bind to EcR to be able to exert antagonistic effects on this receptor. CASTp server is routinely used to computationally identify binding pockets within proteins (Tian et al., 2018). Amino acid composition of the predicted the binding site of EcR determined by the CASTp server are as follows: Ala374, Lys377, Ala378, Ser381, Glu382, Glu452, Arg453, Pro454, Ser455, Arg500, Gly503, Asn504, Asn506, Ser507, Trp528, Asp529.

Table 1. Summary of *in silico* predictions of physicochemical properties, secondary structures and topology for ecdysone receptor from *Schistocerca gregaria* (Accession number: A0A109P395).

Tools	Parameters	Values
ProtParam	Number of amino acids (AA)	532
	Molecular weight (Mw)	58194.43
	Theoretical isoelectric point (pI)	8.23
	Total number of negatively charged residues (Asp+Glu)	65
	Total number of positively charged residues (Arg+Lys)	69
	Instability index	58.64
	Aliphatic index	75.47
	GRAVY[a]	-0.394
SOPMA	α-helix (%)	36.28
	β-strand (%)	10.71
	β-turn (%)	6.02
	Random coil (%)	46.99
TMHMM	Number of predicted TMHs[b]	0
	Expected number of AAs in TMHs[c]	0.39486
	Expected number of helices, first 60 AAs[d]	0.39162
	Total probability of N-in[e]	0.01754

[a]Grand average of hydropathicity index.
[b]The number of predicted transmembrane helices.
[c]The expected number of amino acids in transmembrane helices.
[d]The expected number of amino acids in transmembrane helices in the first 60 amino acids of the protein.
[e]The total probability that the N-terminal end is on the cytoplasmic side of the membrane.

Validation of predicted 3D structural model

To study the binding mode and affinity of the selected protease inhibitors with EcR using HADDOCK, 3D structures of proteins are needed (in PDB format). Publicly available 3D structures of protease inhibitors were retrieved from PDB archive. However, no experimental structure was available for the desert locust EcR, and we used SWISS-MODEL server to generate a 3D structural model for this protein. Alignment of the amino acid sequence of EcR (the target protein) against SMTL resulted in a set of 50 templates with high sequence coverage and sequence identities. From the models calculated on the basis of different templates, the best homology model was selected according to GMQE and QMEANDisco global and QMEAN scores (Table 2). The GMQE score around 0 and the QMEANDisCo global score below 0.6 indicate the low overall quality of predicted models. In this study, the model generated on the basis of the crystal structure of EcR/USP heterodimer from a sheep body louse (Ren et al., 2014) with the PDB accession number of 4OZT and the sequence identity of 92.27% to the target protein had a GMQE score of 0.23 and an excellent QMEANDisCo global score of 0.81, and was therefore considered to be of good quality and was subjected to further quality assessments.

The absolute quality of the selected model was measured based on the QMEAN Z-score. A QMEAN Z-score around 0 indicates the excellent quality of predicted models, whereas values below –4 are indicative of models with low quality. The QMEAN Z-score of the selected model was calculated to be 0.21, which indicates a good agreement between the template and the homology model.

The quality of the generated model was further evaluated using SAVES tools (PROCHECK, ERRAT, and VERIFY 3D) and PROSA (Table 2). Ramachandran plot generated by PROCHECK, which shows the distribution of torsional angles (phi (φ) and psi (ψ)) in the model, estimated that most of the residues (93.9%) clustered in the 'most favored' region, whereas a small percentage of residues occurred in the 'additional allowed' (5.6%), the 'generously allowed' (0.6%) and the 'disallowed'

Table 2. Quality assessment of the predicted 3D model of the ecdysone receptor from Schistocerca gregaria (Accession number: A0A109P395).

Tools	Parameter(s)		Values
Protein Geometry	MolProbity Score		1.26
	Clash Score		0.94
	Ramachandran outliers		1.04%
	Ramachandran favored		97.92%
	Rotamer Outliers		4.02%
	Cβ deviation>0.25Å		1
	Bad bonds		0/1608
	Bad angles		5/2166
Peptide Omegas	Cis Prolines		1/6
Model Evaluation	GMQE		0.23
	QMEANDisCo Global		0.81
	QMEAN Z-Scores	QMEAN	0.21
		C_beta interaction energy	0.80
		All-atom pairwise energy	1.48
		Solvation energy	1.58
		Torsion angle energy	-0.68
SAVES	PROCHECK		93.90%
	VERIFY		95.36%
	ERRAT		99.46

(0%) regions (Fig. 1A). The structure was then verified by VERIFY 3D, which found that 95.4% of residues of the model had an average 3D-1D score greater than 0.2. The overall quality of non-bonded interactions in the protein structure calculated by ERRAT was found to be approximately 99.5%, which is within the acceptable range (>50). The PROSA Z-score was calculated to be –7.63 (Fig. 1B, C), a value within the range of experimental native structures of similar sizes, further validating the overall quality of the model. In conclusion, the predicted 3D structure for the desert locust EcR was found to be reasonably reliable to conduct docking studies (Fig. 1D).

Docking of inhibitors with EcR

The ability of the locust-derived protease inhibitors to interact with the binding site of the desert locust EcR was investigated by performing docking studies using the HADDOCK webserver (Table 3). Grouping of refined structures based on interface-ligand RMSD similarity resulted in x of clusters, which were ranked according to the HADDOCK score. The HADDOCK score is defined as a weighted sum of several energy terms, including electrostatic, van der Waals, restraint energies, empirical desolvation potential as well as the buried surface area.

All the eight tested inhibitors showed the ability to bind to EcR. However, the inhibitor derived from the serine protease inhibitor (SGTI) of *S. gregaria* (designated 1KJ0) was calculated to have the lowest values of total energy (−473.24 kcal/mol), HADDOCK score (−118.5), binding energy (−10.6 kcal/mol), dissociation constant (8.0E-08 M), and RMSD (1.8 Å). Furthermore, the buried surface area for 1KJ0 on the binding site residues of the EcR was estimated to be 2026.76 $Å^2$. In conclusion, 1KJ0 was shown to achieve the optimum HADDOCK score, cluster rank, cluster size, RMSD, total docking energy, binding energy, and dissociation constant, indicating that this peptide has the highest predicted binding affinity to the target protein (Table 3).

1KJ0-7 was shown to form 15 intermolecular hydrogen bonding interactions and 141 non-bonded contacts with EcR (Table 3; Fig. 2C). The 3D structure of the 1KJ0/EcR complex, as well as the EcR residues involved

in the interaction with the peptide are displayed in Fig. 2A, B. The residues in EcR interacting with 1KJ0 were identified to be Ala439, Arg480, Lys435, Arg481, Tyr432, Asp437, Arg482, Asn438, Arg390, and Arg387 (Fig. 2C). Weak intermolecular interactions (such as hydrogen bonds) play an important role in stabilizing the binding of inhibitors to target molecules. The side chain of Thr16 in the 1KJ0 forms hydrogen bonds with two residues (Asp437 and Asn438) in the binding site of EcR, suggesting that this residue (i.e., Thr16) contributes to the formation of a tight binding interaction with EcR. Other residues in the binding site of EcR, including Leu443, Tyr476, Glu440, Val436, Pro483, Arg482, Arg391, Phe357 and Leu353, were mainly involved in weak interactions other than hydrogen bonds (e.g., van der Waals interactions) (Fig. 2C).

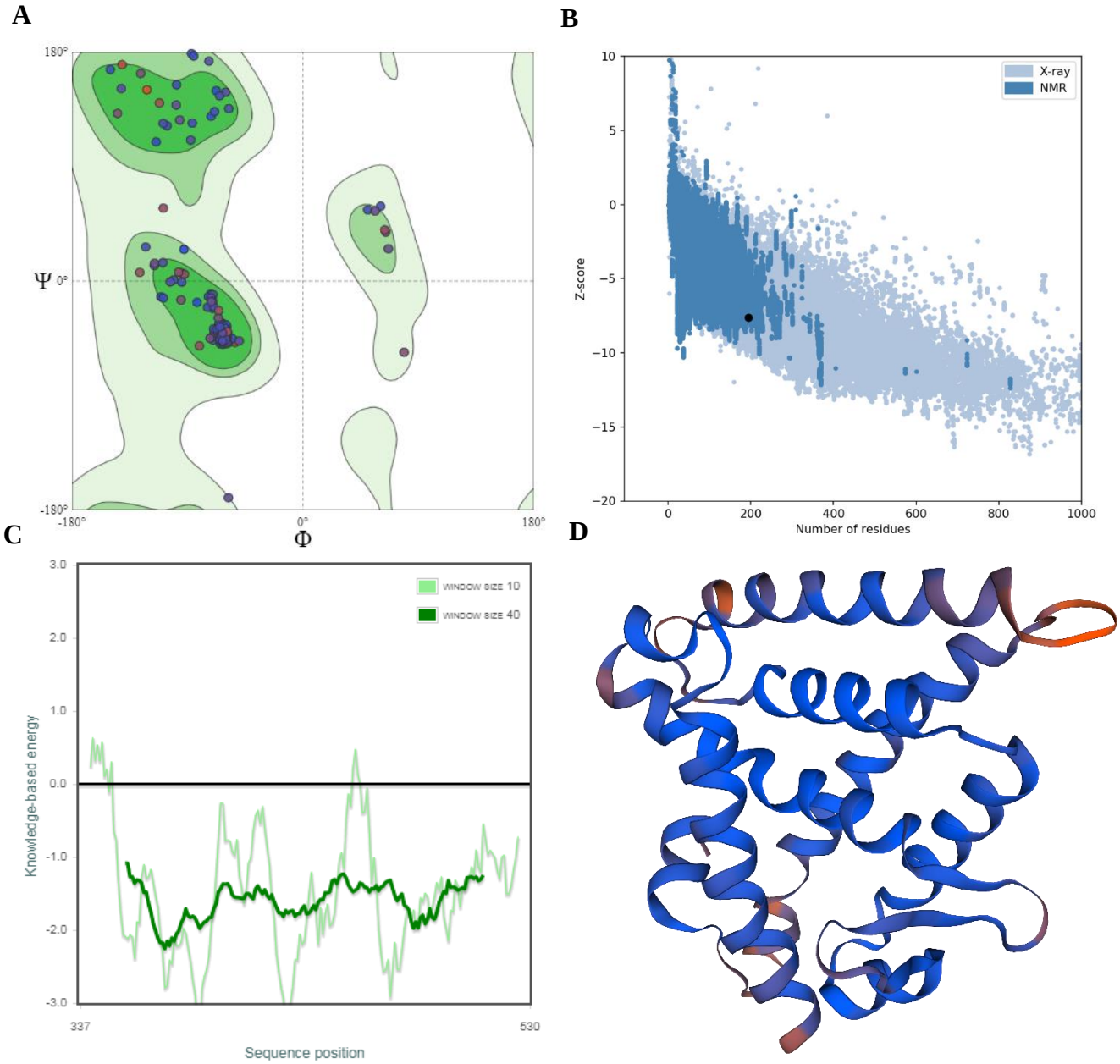

Figure 1. 3D structure validation of the ecdysone receptor from *Schistocerca gregaria*. (A) Ramachandran plot Ramachandran plot of the selected structure, (B) Overall structural model quality on the basis of Z-score (black plot), (C) the local model quality of the selected structure by plotting energies as a function of amino acid sequence position, (D) A ribbon diagram of the selected EcR model. Ramachandran plot was determined by PROCHECK. Z-score was determined by PROSA.

Table 3. Summary of HADDOCK prediction for the interaction of the ecdysone receptor from *Schistocerca gregaria* and various locust-derived protease inhibitors.

Inhibitor PDB ID	Inhibitor length (AA)	Inhibitor characteristic	Insect species	Cluster	HADDOCK score	Cluster size	RMSD (Å)	Z-Score	Energy (kcal/mol)				Buried surface area (Å^2)	$\Delta G_{binding}$ (kcal/mol)	K_d (M)	Hbonds (no.)	Non-bonded contacts (no.)
									Vander Waals	Electrostatic	Desolvation	Total					
1KJ0_A	35	Serine protease inhibitor (SGTI)	*Schistocerca gregaria*	1	-118.5	58	1.8	-2.1	-57.05	-416.18	14.1	-473.24	2026.76	-10.6	8.0E-08	15	141
1KGM_A	35	Serine protease inhibitor (SGCI)	*Schistocerca gregaria*	6	-84.5	6	7.1	-1.4	-60.37	-320.52	4.8	-380.52	1641.66	-9.8	6.8E-08	15	136
2XTT_A	36	Protease inhibitor SGPI-1	*Schistocerca gregaria*	1	-96.8	41	7.2	-1.3	-73.00	-290.00	8.9	-363.01	1800.26	-9.0	2.7E-07	15	127
2VU8_B	33	Protease Inhibitor 3	*Locusta migratoria*	1	-89.5	18	2.2	-1.6	-64.05	-275.82	0.3	-339.87	1946.08	-9.7	1.7E-08	14	119
1KIO_A	35	Serine protease inhibitor (SGCI)	*Schistocerca gregaria*	2	-69.3	11	4.2	-1.6	-61.31	-261.73	-11.1	-323.04	1468.63	-10.3	3.0E-08	14	140
1WO9_A	35	Trypsin inhibitor (HI)	*Locusta migratoria*	3	-94.2	25	1.2	-2.2	-66.06	-214.14	-9.0	-280.20	1781.86	-10.5	1.9E-08	15	121
1GL1_D	36	Protease inhibitor LCMI II	*Locusta migratoria*	1	-90.9	25	5.1	-1.4	-65.36	-208.20	5.3	-273.56	1760.89	-9.4	1.2E-07	8	118
1GL0_B	35	Protease inhibitor LCMI I	*Locusta migratoria*	1	-85.1	31	2.5	-1.4	-78.65	-99.69	-5.40	-178.35	1932.00	-9.5	1.0E-07	6	124

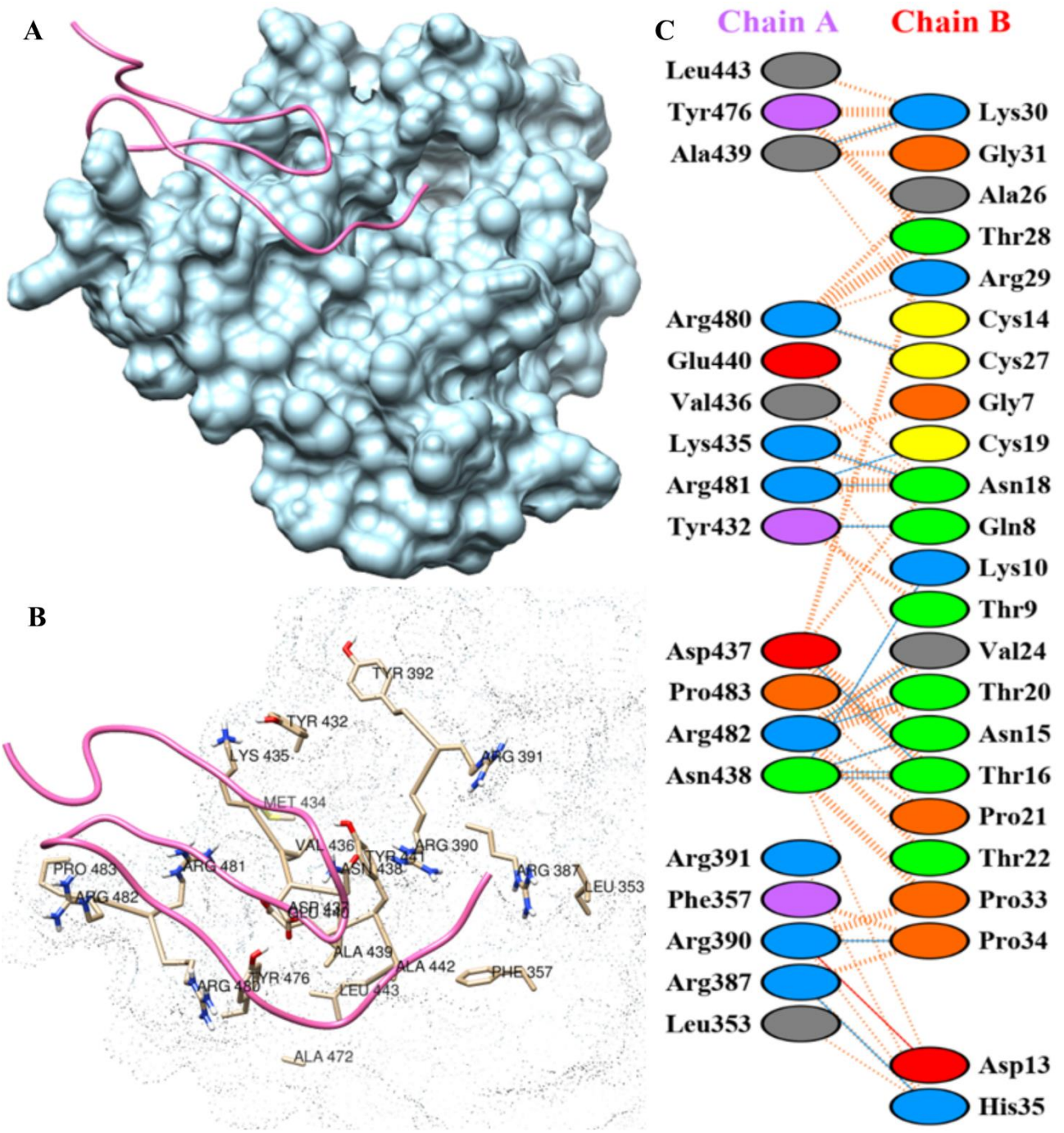

Figure 2. Receptor–inhibitor interaction diagrams. (A) The structure of protease inhibitor (1KJ0) (pink) complexed with the *Schistocerca gregaria* ecdysone receptor (light blue); (B) The interactions between the protease inhibitor (1KJ0) and the residues involved in the receptor binding site, and (C) Individual residue–residue interactions across the interface between the ecdysone receptor of *Schistocerca gregaria* (Chain A) and the protease inhibitor (1KJ0, Chain B). Blue lines and orange tick-marks represent hydrogen bonds and non-bonded contacts.

In this study, we adopted an *in silico* approach to assess the potential binding of eight locust-derived protease inhibitors with the desert locust EcR in order to discover novel antagonistic compounds that could be used in long-term pest management programs. Furthermore, the molecular mechanisms involved in the interactions between the protease inhibitors and EcR were identified using bioinformatics tools. The predicted interactions suggested the antagonistic capacity of the studied inhibitors against EcR, and the

best inhibitor (1KJ0) seems to be a promising candidate as an insecticide to selectively prevent locust-related crop losses. However, laboratory-based investigations are further required to validate the accuracy of the adopted methodology in predicting the interaction of proposed candidates with EcR and demonstrate the efficacy of 1KJ0 as an EcR antagonist. Identification of novel antagonistic compounds offers an interesting opportunity for developing transgenic pest-resistant plants as part of an integrated pest management strategy. Moreover, the findings could pave the way for future insecticides that are specifically designed for pest control.

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شناسایی آنتاگونیست‌های جدید گیرنده اکدایزون ملخ صحرایی، (*Schistocerca gregaria*)، با استفاده از مدل‌سازی محاسباتی

سید علی همتی *

* **نویسنده مسوول:** استادیار گروه گیاه‌پزشکی، دانشکده کشاورزی، دانشگاه شهید چمران اهواز، اهواز، ایران (sa.hemmati@scu.ac.ir)

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چکیده

ملخ صحرایی، *Schistocerca gregaria* Forsskål، به عنوان مخرب‌ترین آفت مهاجر به مناطق وسیعی از زمین‌های زراعی و مراتع در نقاط مختلف جهان خسارت وارد می‌کند. به طور معمول، ملخ‌های صحرایی با استفاده از حشره‌کش‌های شیمیایی کنترل می‌شوند. با این حال، به دلیل اثرات جانبی حشره‌کش‌های رایج بر سلامت انسان، محیط زیست و ظهور حشرات مقاوم به حشره‌کش‌ها، توسعه برنامه‌های جایگزین مدیریت آفت ضروری به نظر می‌رسد. باتوجه به نقش کلیدی گیرنده اکدایزون (EcR) در رشد و نمو حشرات، این مطالعه با هدف استفاده از برنامه‌های محاسباتی در جهت کشف ترکیباتی با ویژگی‌های آنتاگونیستی برای گیرنده اکدایزون ملخ صحرایی صورت پذیرفت. درک ویژگی‌های بیوشیمیایی و ساختاری گیرنده اکدایزون جهت طراحی آنتاگونیست‌های اختصاصی مورد نیاز است و بنابراین در این مطالعه ابتدا خواص فیزیکوشیمیایی، ساختارهای ثانویه و توپولوژی گیرنده اکدایزون ملخ صحرایی با استفاده از برنامه‌های بیوانفورماتیکی مورد بررسی قرار گرفت. مدل‌های ساختاری سه بعدی گیرنده اکدایزون با استفاده از SWISS-MODEL پیش‌بینی شده و کیفیت مدل‌های حاصل با استفاده از برنامه‌های مختلف مورد ارزیابی قرار گرفت. مطالعات داکینگ مولکولی بین هشت مهارکننده پروتئازی مشتق شده از ملخ‌ها و مدل پیش‌بینی شده گیرنده اکدایزون نشان‌دهنده پتانسیل مطلوب آنتاگونیستی همه مهارکننده‌های مورد مطالعه در برابر گیرنده اکدایزون بود. با این وجود، مهارکننده 1KJ0 در میان‌کنش با گیرنده اکدایزون، مطلوب‌ترین امتیاز داکینگ، انرژی پیوند، ثابت تفکیک، تعداد پیوندهای هیدروژنی و ارتباطات غیرپیوندی را از خود بروز داد که حاکی از پتانسیل آنتاگونیستی بالای 1KJ0 در مقابل گیرنده اکدایزون بود. نتایج حاصل از این پژوهش، اهمیت مطالعات محاسباتی را در شناسایی آنتاگونیست‌های جدید علیه پروتئین هدف را نشان می‌دهد. با این حال، تحقیقات *in vitro* و *in vivo* جهت اعتبار بخشیدن به ترکیب معرفی شده مورد نیاز است.

***کلیدواژه‌ها: Schistocerca gregaria*، مهارکننده‌های پروتئازی ملخ، داکینگ مولکولی، مدیریت آفت**

دبیر تخصصی: دکتر محمد مهرآبادی

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