ISSN: 2459-425X • Website: www.ijrstms.com

## In SILICO Molecular Docking of Kappa-Carageenan Against D7 Salivary Gland Protein of Adult Female Anopheles Stephesnsi

**Prof.Aravind Prasad** 

<sup>\*1</sup>Department of Microbiology and Biotechnology, Faculty of Arts and Science, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India

### ABSTRACT

The purpose of this study was to analyze the inhibitory action of Kappa carrageenan by computational docking simulation studies. For this, natural metabolite Kappa-carrageenan was used as ligand for molecular interaction. Computational docking analysis was performed using Arguslab and Pymol based on scoring functions. Kappa-carrageenan compound showed high docking potential with the D7 salivary gland protein of female *Anopheles stephensi*. The results clearly show that the molecular docking mechanism used to detect the novel antirepellant for mosquito has been successfully obtained from a natural sulfated polysaccharide compound.

*Key words:* D7 salivary gland protein, Anopheles stephensi, Kappa-carrageenan, Molecular docking.

#### **INTRODUCTION**

Carrageenan is a common name for the family of gel-forming and viscous polysaccharides, derived from some species of red seaweed [1]. Carrageenan is derived from a number of seaweeds of the class Rhodophyceae. This unique seaweed is common in the Atlantic Ocean near Britain, Europe and North America. When used in food products, carrageenan contains the EU additive E-number E407 or E407a. The E407a has a slightly different composition; moreover, it contains considerable cellulose. Carrageenan has no nutritional value and is used in food preparation for its gelling, hardening and emulsifying properties and experimental medicine this substance is often used for the testing of anti-inflammatory, antitumor, antimicrobial, antiviral (HSV) and antithrombin agents [2-6]. Keeping the above medicinal properties in mind we are the first pioneer

#### ISSN: 2459-425X • Website: www.ijrstms.com

to identify the *in silico* molecular docking potential of Kappa-carrageenan compound against D7 salivary gland protein of *Anopheles stephensi*.

## MATERIALS AND METHODS Preparation of protein structure SwissProt (URL: http://expasy.org/sprot/)

The UniProt/Swissprot Knowledgebase (UniProtKB) (Fig. 1) is the central access point for extensive curated protein information, including function, classification, and cross-reference. It consists of two sections: UniProtKB/Swiss-Prot which is manually annotated and is reviewed and UniProtKB/TrEMBL which is automatically annotated and is not reviewed. The UniProt Reference Clusters (UniRef) databases provide clustered sets of sequences from the UniProtKB and selected UniProt Archive records to obtain complete coverage of sequence space at several resolutions while hiding redundant sequences.

ExPASy	Documents	Hune ( Conset
UniProtKB/Swiss-Prot		
UniProt(B/3/swise-Prot is the manually annotated and It is a high quality annotated and non-redundant prot conclusions. Since 2002, it is maintained by the UniProt consortiu	I reviewed section of the UniProt Knowledgebase (UniProtKB), ain sequence database, which brings together experimental resi m and is accessible via the UniProt website.	utts, computed features and scientific
List of UniProtKB/Swiss-Prot (reviewed) entries Download – UniProt FTP sites. Statistics.		
Additional information:		
<ul> <li>Why is UniProtKB composed of 2 sections. Un</li> <li>Biocuration in UniProt.</li> <li>How do we manually annotate a UniProtKB en</li> <li>UniProt manual annotation program.</li> <li>UniProt general documentation.</li> <li>PAQ.</li> </ul>	iProtKB/Swiss-Prot and UniProtKB/TrEMBL?	
Around UmProd(B/Swiaa-Prot		
NextProt - Exploring the universe of human proteins. Viralzone - A portal to viral UniProtKB/Swiss-Prot en HAMAP - High-quality Automated and Manuel Annot SwissVar - A portal to Swiss-Prot diseases and van UniPratiway - A metabolic door to UniProtKB/Swiss- Enzyme - A repository of Information relative to the r	ntres. ation of microbial Proteomes ants. Prot. nomenclature of enzymes.	
Swiss-Shop - A service that allows you to automatic	ally obtain (by email) new UniProtKB/Swiss-Prot entries relevan	t to your field(s) of interest.
Protein Spotlight - One month, one protein. Proteomics tools		
Contact Le		

### Fig. 1: SwissProt home page

ISSN: 2459-425X • Website: www.ijrstms.com

#### Protein Data Bank (URL: http://www.rcsb.org/pdb/home/home.do)

The Protein Data Bank is a repository for the 3-D structural data of large biological molecules, such as proteins and nucleic acids. The data, typically obtained by X-ray crystallography or NMR spectroscopy and submitted by biologists and biochemists from around the world, are freely accessible on the Internet via the websites of its member organizations (PDBe, PDBj, and RCSB). The PDB is overseen by an organization called the Worldwide Protein Data Bank, wwPDB. The PDB is a key resource in areas of structural biology, such as structural genomics. Most major scientific journals, and some funding agencies, such as the NIH in the USA, now require scientists to submit their structure data to the PDB (Fig. 2).



Fig. 2: PDB homepage

PubMed (http://www.ncbi.nlm.nih.gov/pubmed/)

PubMed is a free database accessing the MEDLINE database of citations, abstracts and some full text articles on life sciences and biomedical topics. The United States National Library of Medicine (NLM) at the National Institutes of Health (NIH) maintains PubMed (Fig. 3,4 and 5) as part of the Entrez information retrieval system.

ISSN: 2459-425X • Website: www.ijrstms.com

S NCBI Resources	🖲 now to 🕑				Singer and No. NG BK
Publiced (	Publied •				(Search) Herp
	PubMed PubMet comprise MEDLINE, life sois content from Publ	s more than 22 million citations for biomedical i nice journals, and online books. Citations may i led Central and publisher web sites.	Nerature from Include links to halk text	PubReader A visit new way to red visitilit Iterator of Fuldwai (secol	
Using PubMed		PubMed Tools		More Resource	05
PUCKHED QUICK STARS GUT	de.	Publied Mobile		MeSH Database	
Eul Test Articles	Cies Single Citation Matche			Journals in NCBI Databases	
PubMed FAQs		Batch Clution Matchet		Cinca Trata	
PubMed Tutoriate		Cinical Operant		E-Utilites	
New and Noteworthy		Tops: Specific Guerani		LinnQut	
You are here. NCBL> Litera	tµe > Publied				With its The Help Door
GETTING STARTED NGR Education NGR Hap Markal NGR Hap Markal NGR Handoosh Training & Tuterian	RESOURCES Chemically & Research Data & Schware Drank Rola Domany & Stauchare Canadi & Excession Genetics & Nettone Genetics & Nettone Genetics & Nettone Genetics & Nettone Genetics & Nettone	POPULAR Publies Nacio0358 BLADT Phated Lentes Gane Bocipties Protes OWER Genome	FEATURED Generals Charat Pacifica Charat Generals Realing Charat Rain Woool Harmon Elecon Moreia Genorn Moreia Harat Prome-BLAST	g-Recardo n guerona guerona N	NCBI INFORMATION Information Report at NCBI NDBI Hereistetter NDBI FTP Mer NDBI of Facebook NCBI of Techuse NCBI of Yechuse





## Fig. 4: Retrieve of D7 protein sequence chain view from PDB **QPWKALDAEQ ALYVYKRCYE DHLPSGSDRK TYMTLWNAWR LEPNDAITHC** 1 ННН ННННННННН ННЅ ЅЅТННН ННННННТТ ЅЅЅННННН YAKCVLTGLQ IYDPQENAFK SDRIPVQYQA YKTITQSKQK EVTEYQKALA 51 НННННННТТ SEETTTTEE ТТННННННН ННННН НН ННННННННН 101 AANAKSGSCV DLYNAYLPVH NRFVNLSRQL YHGTVEGAAK IYAAMPEIKQ Н ТТ НН НННННННН НННННННН ТТ ЅННННН НННН ТТЅ 151 KGESFHAYCE KRAWKGNKQS EWKNGRRYKL TGSPELKDAI DCIFRGLRYM TTB HHHHHH HHHS SSS TTTTS ННННННН ННННННТТЅЕ 201 DDTGLKVDEI VRDFNLINKS ELEPEVRSVL ASCKGSEAYD YYVCLVNSRL ETTEE HHHH HHHHHHTT G GGHHHHHHHH HT S SHHH HHHHHHTSTT

251 KQHFKNAFDF HELRSADYAY LLRGKVYENP EKVKEEMKKL NTTVHF HHHHHHHHHHHHHHHTTT T H HHHHHHHTS BS

ISSN: 2459-425X • Website: www.ijrstms.com

#### Fig.5: Sequence of D7 protein and secondary structure was retrieved from PDB

#### PubChem Database (URL: <u>http://pubchem.ncbi.nlm.nih.gov/</u>)

The PubChem Substances Database contains descriptions of chemical samples, from a variety of sources, and links to PubMed citations, protein 3D structures, and biological screening results that are available in PubChem BioAssay. If the contents of a chemical sample are known, the description includes links to PubChem Compound (Fig. 6).

	Bioactivity Q summary
	Bioactivity datatable
Pub©hem	Bioactivity structure-activity
	Chemical structure search
🕜 BioAssay 🛛 🔗 Compound 🛛 🍈 Substance 🛛	3D conformer viewer
	Chemical structure clustering
search	Deposition gateway 💡
Chemical structure search   BioActivity analysis	Structure download 🧉
	Bioassay download
w Structures from Immunology Lab, Department of Biotechnology, Calicut Niversity are now available in PubChem.	PubChem FTP
w Structures from AKos are now available in PubChem.	
RNAi screening data and substances from the Drosophila RNAi Screening	
RNAi screening data and substances from the Drosophila RNAi Screening enter (DRSC) are now available in PubChem.	

Fig. 6: PubChem home page

### RasMol

RasMol (Fig. 7) is a computer program written for molecular graphics visualization intended and used primarily for the depiction and exploration of biological macromolecule structures, such as those found in the Protein Data Bank. It was originally developed by Roger Sayle in the early 90s. It was an important tool for molecular biologists since the extremely optimized program allowed the software to run on (then) modestly powerful personal computers. Before RasMol, visualization software ran on graphics workstations that, due to their expense,

#### ISSN: 2459-425X • Website: www.ijrstms.com

were less accessible to scholars. RasMol has become an important educational tool as well as continuing to be an important tool for research in structural biology.



Fig. 7: RasMol tool page

### **Chem Sketch**

ACD/ChemSketch is an advanced chemical drawing tool and is the accepted interface for the industries best NMR and molecular property predictions, nomenclature, and analytical data handling software. ACD/ChemSketch is also available as freeware, with functionalities that are highly competitive with other popular commercial software packages. The freeware contains tools for 2D structure cleaning, 3D optimization and viewing (Fig. 8).

ISSN: 2459-425X • Website: www.ijrstms.com



#### Fig. 8: Chem Sketch work space

#### Open Babel (<u>http://openbabel.org/wiki/Main\_Page</u>)

Open Babel is a chemical toolbox designed to speak the many languages of chemical data. It's an open, collaborative project allowing anyone to search, convert, analyze, or store data from molecular modeling, chemistry, solid-state materials, biochemistry, or related areas as shown in the figure 9.



ISSN: 2459-425X • Website: www.ijrstms.com

#### Fig. 9: Open Babel tool page

#### ArgusLab

ArgusLab is a program to build graphic representations of molecular models. Using this program, you will be able to show molecular models to pupils, or even design matters by combining different elements. You will be able to include in your model several atoms, residues, groups and calculations (Fig. 10).

PyMol (http://download.cnet.com/PyMOL/3000-2054\_4-10914845.html)

PyMol is an open-source, user-sponsored, molecular visualization system created by Warren Lyford DeLano and commercialized by DeLano Scientific LLC, which is a private software company dedicated to creating useful tools that become universally accessible to scientific and educational communities (Fig. 11).



ISSN: 2459-425X • Website: www.ijrstms.com





ISSN: 2459-425X • Website: www.ijrstms.com

#### Fig. 11: PyMol tool page RESULTS AND DISCUSSION

Protein Name: D7 protein

PDB ID: 3NGV

Alternative name(s): Long form D7clu2 salivary protein

Swissprot ID: Q95NY5 Organism:

Anopheles stephensi Fasta

#### Sequence:

>tr|Q95NY5|Q95NY5\_ANOST D7 protein OS=Anopheles stephensi PE=1 SV=1 MIIVAVLLSFLAHLLVQASQPWKALDAEQALYVYKRCYEDHLPSGSDRKTYMTLWNAWRL EPNDAITHCYAKCVLTGLQIYDPQENAFKSDRIPVQYQAYKTITQSKQKEVTEYQKALAA ANAKSGSCVDLYNAYLPVHNRFVNLSRQLYHGTVEGAAKIYAAMPEIKQKGESFHAYCEK RAWKGNKQSEWKNGRRYKLTGSPELKDAIDCIFRGLRYMDDTGLKVDEIVRDFNLINKSE LEPEVRSVLASCKGSEAYDYYVCLVNSRLKQHFKNAFDFHELRSADYAYLLRGKVYENPE KVKEEMKKLNTTVHF

Jacob Contractor Contractor	
Protein names	Submitted name: D7 protein (EMBL CACTURED 1) Submitted name: Long form D7chu2 salivary protein (EMBL A4LINOLE 1)
Organism	Anopheles stephensi (Indo-Pakistan malaria mosquito) (EHELCHETTED )
Taxonomic identifier	3K069 PVCBQ
Taxonomic lineage	Eskaryota ) Metazoa » Ecidysozoa » Antinopoda » Hexapoda » Inaecta » Pierygota » Neoptera » Endopterygota » Diptera » Nematocera » Culicidae » Culicidae » Anophelinae » Anopheles » 🎟
Protein attributes	
Sequence length	315 AA
Sequence status	Complete.
Sequence processing	The displayed sequence is further processed into a mature form.
Protein existence	Evidence at protein level
Ontologies	
Keywords	
Domain	Signal (EBR. DALTARE)
Technical term	30-structure (PER MAT) (PER MAT)
Gene Ontology (GO)	
Molecular_function	odorant binding Interned from electronic annotation. Source: InterPro

ISSN: 2459-425X • Website: www.ijrstms.com

## Fig. 12: SwissProt entry page



Fig. 13: Visualization of D7 protein using Rasmol tool



Fig. 14: 2D structure of kappa-carragennan

ISSN: 2459-425X • Website: www.ijrstms.com



Fig. 15: 3D structure of kappa-carragennan



Fig. 16: Grid setting of D7 protein using ArgusLab

ISSN: 2459-425X • Website: www.ijrstms.com



Fig. 17: Visualization of docked complex of kappa-carragennan with D7 protein

D7 pro	tein	Kappa-carragennan	Docking score KCal/mol	Distance (Å)	H-Bond
ARG 74	NH2	Ο	-8.67	2.9	10
TRP 4	N	Ο		3.0	
GLN 2	0	Н		2.3	
LYS 5	N	О		3.1	
ALA 6	0	0		3.2	
GLN 61	NE2	0		2.7	
GLN 61	NE2	0		3.0	
GLN 11	NE2	0		3.0	
GLN 11	NE2	0		2.9	
ARG 199	NE	0		2.3	

## Table 1: Docked complex of kappa-carragennan with D7 protein

ISSN: 2459-425X • Website: www.ijrstms.com

To study the binding mode of kappa-carragennan interaction with D7 protein, intermolecular flexible docking simulations were performed and. Energy values were calculated from the docked conformations of the protein-inhibitor complexes. Docking studies yielded crucial information concerning the orientation of the inhibitors in the binding pocket of the target protein. Several potential inhibitors have been identified through the docking simulation. The binding affinity of the D7 protein with the kappa-carragennan was measured by kcal/mol. The docking score was found to be -8.67 kcal/mol with the stronger interaction as showed in the table 1 and fig. 17. Analysis of ligand binding interaction with the protein can be useful for the antirepllant activity against *Anopheles stephensi* mosquito. The results obtained from this study would be useful in both understanding the inhibitory mode as well as in rapidly and accurately predicting the activities of larvicidal on the basis of docking scores.

This is the first study to demonstrate the docking simulation of sulphated polysacride (kappacarragennan) against *Anopheles stephensi* mosquito protein Our results showed that the presence of the hydrobic interaction with 10 hydrogen bond with the interaction of ligand to form a docked complex.. This research supports the novel idelogical use of kappa-carragennan as an alternative insecticide for the control of *Anopheles stephensi* mosquito, which is a vector of severe arboviruses, such as dengue and chikungunya. Similar observations were observed by Diégina *et al.* (2019) [7] by using H. velutina extracts against Aedes aegypti and his docking results prove to valid by producing high docking score of 103.02 kcal/mol against the A. aegypti mosquito protein (1PZ4 protein).

#### Conclusion

In this study, the molecular docking was applied to explore the binding mechanism and to correlate its docking score with the activity of kappa-carragennan. The results of our present study can be useful for the design and development of novel compound having better inhibitory activity against the control of mosquito prevalence in the world. These potential drug candidates can further be validated in wet lab studies for its proper function.