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HOMOLOGY MODELLING AND ANALYSIS OF PROTEIN DRUG TARGETS FOR *ERYSIPELOTHRIX RHUSIOPATHIAE* A BACTERIAL PATHOGEN CAUSING SWINE ERYSIPELAS

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Keywords:

Homology modelling, *Erysipelothrix rhusiopathiae*, Protein Drug Targets, Swine erysipelas

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ABSTRACT: Aim of this study was to generate 3D models of protein drug targets in *Erysipelothrix rhusiopathiae* by homology modelling. *E. rhusiopathiae* causes swine erysipelas disease that has great economic impact on the pork industry. Bioinformatic databases such as Uniprot KB, Drug Bank, PMDB and online tools such as BLASTp, SWISS Model and Ramachandran plot analysis and software such as Autodock4 and Pymol were used to perform this study. Among 4153 proteins reported from *Erysipelothrix rhusiopathiae*, 396 proteins were identified as potential drug targets. These 396 proteins were employed in homology modelling through the SWISS Model. Total of 131 homology structures with the Ramachandran favorable score above 95% were considered as reliable drug targets and were submitted to PMDB online database. The modelled proteins were subjected to protein-ligand docking analysis with standard antibiotics such as Ribostamycin, Cefalotin, Pefloxacin, Penicillamine, Artenimol, Cycloserine against their respective drug targets. Among these antibiotics Ribostamycin was identified as a potent drug against the Protein Disulphide Isomerase with a significant binding energy of -7.35Kcal/mol with formation of 5 hydrogen bonds. The docking results suggest that the infection of *Erysipelothrix rhusiopathiae* could be treated with Ribostamycin antibiotic. The homology model of the proteins generated in this study can be exploited in further research using computational drug discovery and design to accelerate the research on disease management and pathogen control of *Erysipelothrix rhusiopathiae* induced swine erysipelas.

INTRODUCTION: The pork sector has immensely contributed to the farming and agriculture economy. Development in the swine industry is mainly because of advancements in genetics and breeding, improved farming techniques and better management practices.

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About one-third of meat consumed in the world is pork [1]. Pig meat production was around 117 million tonnes in 2015 and is expected to reach 127 million tonnes in 2025, growing at 1.4% [2]. Asia, Europe, and North America contribute 80% towards pig meat production [1].

China is the largest pork producer and contributes about 50% of the world's pork production [1]. The second-largest producer of pork is the European Union, and it is the largest exporter [2]. *Erysipelothrix rhusiopathiae* is a rod-shaped Gram-positive bacterium.

It is responsible for causing erysipelas in a wide range of vertebrate animals. The bacteria is zoonotic and hence can cause severe outbreaks [3]. Koch first isolated the bacteria in 1876, and he described the organism as 'bacillus of mouse septicaemia' and was named *E. muriseptica* as he inoculated it from a mouse's putrefied blood. Loeffer was the one to provide a detailed report on the bacteria and the infection caused by it. He studied the cutaneous blood from a pig that died due to erysipelas in 1882. The disease erysipelas was first confused with anthrax, but with further studies, the causative organism was found to be a bacillus rather than a streptococcus. The presence of erysipelas was revealed in the United States due to the efforts of Theobold Smith while he was working for the Bureau of Animal Industry before the 1900s. In 1921 G.T Screech established the relationship between Diamond skin disease, a clinical form of erysipelas, and *Erysipelothrix rhusiopathiae* [4].

The organism *Erysipelothrix rhusiopathiae* causes infection in the absence of specific antibodies and by evading the phagocytotic cells. Even on being phagocytised this pathogen can replicate intracellularly within these cells. This property demonstrates the capacity of the bacteria to survive intracellularly [5].

The *Erysipilothrix rhusiopathiae* usually enters the host through contaminated food. It was found that approximately 30-50% of healthy swine carry these organisms. These organisms are usually found in the tonsils and other lymphoid tissues of the alimentary canal of the host organism [6].

Erysipelothrix rhusiopathiae is a Gram-positive, non-spore-forming, non-acid fast, rod-shaped bacterium. The bacteria have a capsule that contributes to their virulence. The capsule polysaccharide forms the major non-protein antigen. There are various enzymes involved in the pathogenicity of the bacteria; neuraminidase is one such enzyme produced by the organism that causes the release of terminal sialic acid residues from glycoproteins, glycolipid, oligosaccharides of the host cell. The organism also produces hyaluronidase, a spreading factor that contributes to the bacteria's spread into tissues [6]. The spread of *Erysipilothrix rhusiopathiae* is very difficult to control as the bacteria are zoonotic and can spread to other animals and humans (occupational hazard). Even though the bacteria affects almost all the vertebrates, the study of the bacteria is not as widespread as estimated, and very little information is available on the bacteria, it's structure and its pathogenicity. Bioinformatics conceptualizes biology in terms of molecules and utilizes informatics techniques to understand and organize these molecules. The aim for bioinformatics is to (i) To organize data to make it easier for researchers to access information and submit new information (ii) To develop tools and resources that help in the analysis of data (iii) To analyze and interpret data in a biologically meaningful manner. Homology modelling allows valuable insights into the molecular basis of protein function; here we are using it to identify drug targets that will help in developing a potential cure for the disease. The SWISS-MODEL Automated is one of the homology modelling tools which develops automated protein models for a given template or amino acid sequence [7, 8].

MATERIALS & METHODS:

NCBI Database: This website was looked upon to derive the known data regarding the organism of interest. A detailed search on the organism disclosed the available data from several databases. (https://www.ncbi.nlm.nih.gov/)

Sequence Retrieval: A consolidated, publicly accessible online website was referred to get the preferred amino acid sequences for further research [9]. The name of the organism was used as the main criteria which could retrieve the best sequences, which were later sorted according to the length of the amino acid chain and were downloaded in a specific format called fasta. The sequences were checked and verified for duplicates. Duplicates were deleted to avoid confusion, and downloaded sequences were sorted along with their respective Uniprot IDs. (www.uniprot.org) [9].

Sequence Alignment: The amino acid sequences or query sequences procured from the UNIPROT (www.uniprot.org) were all collated with the BLASTp server, which contrasts the query sequence with the pre-existing protein sequences in the Protein Data Bank to obtain a likeness in percentages. The first BLAST search is performed

to get resemblance values with pre-existing sequences. The second BLAST search follows this to get similar values with sequences present in the Protein Data Bank (www.rcsb.org). The similarity approximation obtained in percentages was noted down for further study [10].

Structural Prediction: The 3D structure of the desired drug target proteins are predicted through homology modelling technique, using the online tool Swiss-Model (https://swissmodel.expasy.org/). This tool utilizes respective amino acid sequences of the protein as well as the templates present in the protein databank to predict 3D protein structure. Sequences got from UNIPROT were uploaded in fasta format, and the predicted 3D models were saved in pdb file format. The developed model quality depended on the availability and percentage similarities of the templates. The Ramachandran plots were used to analyze the developed 3D models, which are the graphical plots of protein structures that confirm the precision of the predicted structure in terms of torsion angles. After completion of the analysis, the best models procured were saved in pdb file format [11–13].

Model Analysis: The validity of the expected model was tested and executed through the Ramachandran plot given by the SWISS-MODEL. The degree angles of all the residues were anticipated to be within the Most-Favored regions of the Ramachandran plot establishing the quality of the predicted structure. The residues outside the favored regions were considered to be outliers or unfavored predictions [11, 13].

Model Submission: The 3D models predicted with the preferred Ramachandran plot (favored region) were uploaded to the public database, *i.e.*, Protein Model Data Base (PMDB) [https://bioinformatics.cineca.it/PMDB/] that keeps manually constructed protein models. The 3D models are put up in a specific format of a file called pdb, and the NR ids are generated through the BLAST search; if unavailable, the entries are manually updated, and conclusively, a unique PMDBID is generated. In the final step, interactions between protein and ligand are analyzed using PYMOL, followed by protein-ligand docking in Autodock 4, a molecular modeling simulation software [14].

RESULTS & DISCUSSION:

Pathogen and Drug Selection: The pathogen *Erysipelothrix rhusiopathiae* was selected for the homology modelling studies. There were no reported protein structures of the organism available in the NCBI database. However, 4153 protein sequences were reported in the UniProt KB database (www.uniprot.org). Therefore, the organism chosen was apt to build protein models. Among 4153 protein sequences, the sequences that contained non-enzymatic protein parts, such as ribosomal subunits 900 enzymatic protein sequences, were further analyzed. The protein was searched in the Drug Bank database to check if these 900 protein sequences were reported as drug targets (www.drungbank.ca). Among 900 proteins, 396 proteins were recognized as potential drug targets. These proteins were further subjected to homology modelling.

Building Homology Model: The selected 396 protein sequences were retrieved from the Uniprot database (www.uniprot.org) and were saved in fasta file format (fasta). These sequences were later subjected to known as Protein Blast (Blastp) (https://blast.ncbi.nlm.nih.gov/) to search within the Protein Data Bank (www.rcsb.org) to recognize the templates for Homology Modelling. Protein structures with more than 80% sequence similarity were selected as the ideal template. All 396 had significant sequence similarities, with more than 80% match with existing protein entries on the Protein Data Bank website. The 396 protein sequences were further subjected to building computational homology models using these identified similarity structures. Homology models were constructed using the online web tool SWISS Model (https://swissmodel.expasy.org/). The web tool could construct multiple models for each protein. Among the protein models, the best one was selected based on the sequence coverage (Sequence Identity), and Ramachandran plot analysis, and the Ramachandran favoured region was noted down.

Ramachandran Plot Analysis: The quality of the protein models was evaluated based on their Ramachandran plots.

This analysis was done for 396 drug targets. The models were built using the SwissModel tool. Of

the models generated, the one with its highest number of residues lying in the most preferred regions on the Ramachandran plot was selected. This process was done for each protein. 131 sequences with Ramachandran scores above 95% were considered drug targets and submitted to PMDB. The plots of the proteins with the least confident score (80.79%) ATP-dependent DNA helicase RecG and the most confident score (100.00%) ATP synthase subunit b are graphically interpreted in **Fig. 1.**

Submission to PMDB: A total of 396 homology models were developed through the Swiss-Model interactive workspace out of which only 131 were found favourable by Ramachandran plot analysis i.e., with a Ramachandran score above 95%.

These favoured protein sequences were submitted to Protein Model DataBase (https://bioinformatics.cineca.it/ PMDB/) for cataloging and improvements to be made to the structures.

All models were uploaded in pdb file formats with relevant details and unique PMDB IDs for references and quick searching. **Table 1** shows the list of proteins submitted with their Uniprot IDs, Ramachandran scores, and PMDB IDs.

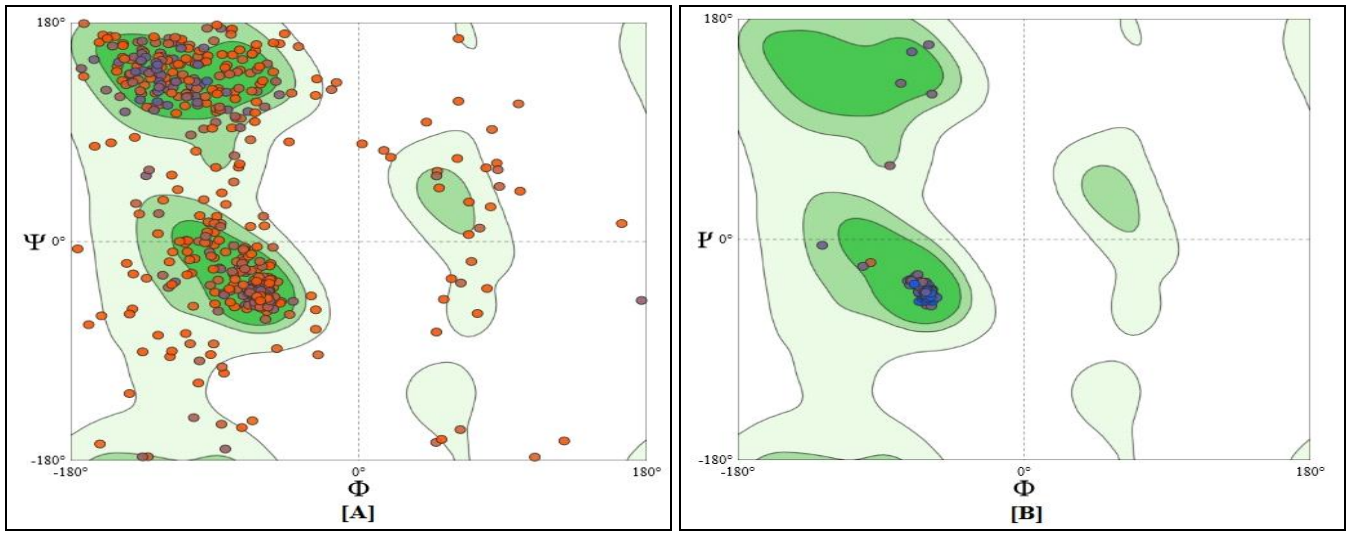

FIG. 1: RAMACHANDRAN PLOT ANALYSIS OF; [A]: LEAST FAVOURED MODEL WITH LOWEST FAVOURABLE SCORE OF 80.79% (ATP-DEPENDENT DNA HELICASE RECG); [B]: MOST FAVOURED MODEL WITH HIGHEST FAVOURABLE SCORE OF 100.00% (ATP SYNTHASE SUBUNIT B)

TABLE 1: LIST OF PROTEIN DRUG TARGETS SUBMITTED TO PMDB DATABASE

S. no.	Entry No	Drug Target Name	Ramachandran Favoured Region	PMDB ID
1	A0A6M2Y2C3	N-acetylglucosamine-6-phosphate deacetylase	95.01%	PM0083646
2	A0A6M2Y314	Replicative DNA helicase (EC 3.6.4.12)	95.04%	PM0083624
3	O50321	Polypeptide	95.05%	PM0083672
4	A0A6M2Y149	L-ascorbate 6-phosphate lactonase	95.06%	PM0083638
5	A0A6M2Y7E6	GMP synthase [glutamine-hydrolyzing]	95.07%	PM0083647
6	A0A6M2Y2F8	Ribulose-phosphate 3-epimerase	95.07%	PM0084035
7	A0A6M2Y046	CoA-binding protein	95.08%	PM0083645
8	A0A6M2XZJ0	Pyrroline-5-carboxylate reductase	95.08%	PM0083594
9	A0A6S6I601	Glucose-1-phosphate thymidylyltransferase	95.10%	PM0083531
10	A0A6M2Y506	Transketolase	95.11%	PM0084042
11	A0A6M2Y166	D-lactate dehydrogenase	95.12%	PM0083532
12	A0A6M2Y3M5	D-alanyl-D-alanine carboxypeptidase	95.15%	PM0083533
13	W8R7I1	Enolase	95.18%	PM0083535
14	A0A0D5C7J1	Integrase	95.19%	PM0083648
15	A0A6M2Y881	Glycerol-3-phosphate dehydrogenase	95.21%	PM0083646
16	A0A6M2Y0X5	Accessory gene regulator C	95.24%	PM0083621
17	A0A6M2Y4C1	AraC family transcriptional regulator	95.24%	PM0083644
18	A0A6M2Y3J3	Phosphocarrier protein HPr	95.24%	PM0083604

19	A0A6M2Y178	Putative Rho-associated protein kinase 1	95.24%	PM0083577
20	A0A6M2Y5S2	Mannose-6-phosphate isomerase	95.27%	PM0083650
21	A0A385XM27	Mature parasite-infected erythrocyte surface antigen	95.27%	PM0083651
22	A0A6M2Y6B5	6-phosphogluconate dehydrogenase, decarboxylating	95.28%	PM0082602
23	A0A6M2Y0T7	Nuclease	95.28%	PM0083558
24	A0A6M2Y5J2	Adhesin	95.30%	PM0084012
25	A0A6M2Y5U5	Arginine deiminase	95.30%	PM0083641
26	A0A6M2Y013	DNA ligase	95.30%	PM0083537
27	A0A0C5H0S4	Macrolide-lincosamide-streptogramin B resistance protein	95.30%	PM0084025
28	A0A6M2Y4H6	Aspartate aminotransferase	95.31%	PM0083640
29	A0A6M2Y2E8	ABC transporter, ATP-binding protein	95.34%	PM0083619
30	A0A6M2Y327	Single-stranded DNA-binding protein (SSB)	95.34%	PM0084037
31	A0A6M2XZL2	Leucine--tRNA ligase	95.35%	PM0084026
32	A0A6M2Y2G8	N-acetyltransferase GCN5	95.36%	PM0084027
33	A0A6M2Y5H3	NAD-dependent malic enzyme 4	95.37%	PM0084029
34	A0A6M2Y8S5	Mevalonate kinase	95.42%	PM0084030
35	A0A6M2Y6L6	Fumarate hydratase class II	95.45%	PM0083541
36	A0A6M2XZL1	Peptide-methionine (R)-S-oxide reductase	95.45%	PM0083589
37	A0A0D5C6N4	Putative copper chaperone	95.45%	PM0083724
38	A0A0D5C6N4	Putative copper chaperone	95.45%	PM0084034
39	A0A6M2Y653	Riboflavin biosynthesis protein	95.45%	PM0084032
40	A0A6M2Y1R1	Aspartate--tRNA ligase	95.48%	PM0083636
41	A0A0D5C6H9	Putative sigma factor	95.49%	PM0083579
42	A0A6M2Y0M0	Adenine phosphoribosyltransferase	95.51%	PM0084009
43	A0A6M2Y7G5	HTH-type transcriptional regulator GltR	95.55%	PM0084031
44	A0A6M2Y7Q9	Putative flavodoxin	95.59%	PM0083569
45	A0A6M2Y4E3	Uracil phosphoribosyltransferase	95.59%	PM0084048
46	A0A6M2Y4G0	Probable endonuclease 4	95.60%	PM0083674
47	A0A6M2XZ30	Adenine DNA glycosylase	95.62%	PM0084008
48	A0A6M2Y2V5	Ferrichrome ABC transporter	95.62%	PM0083547
49	A0A6M2Y8T4	Alanine acetyltransferase	95.63%	PM0084014
50	A0A6M2Y0G5	GntR family transcriptional regulator	95.65%	PM0084033
51	A0A6M2Y7Y3	Aminoglycoside 6-adenylyltransferase	95.67%	PM0084017
52	A0A6M2Y1C2	Deoxyguanosine kinase	95.69%	PM0083549
53	A0A6M2XZM7	Acyl-CoA N-acyltransferase	95.70%	PM0084006
54	A0A6M2Y1D9	ATP-dependent 6-phosphofructokinase	95.73%	PM0083546
55	A0A6M2Y5J5	Methionyl-tRNA formyltransferase	95.74%	PM0084036
56	A0A6M2Y0Y4	Tyrosine--tRNA ligase	95.75%	PM0084046
57	A0A6M2Y3B9	60 kDa chaperonin	95.79%	PM0083609
58	A0A6M2Y4D0	Lysine--tRNA ligase	95.80%	PM0084039
59	A0A6M2Y6T9	Deoxyribose-phosphate aldolase	95.81%	PM0083550
60	A0A6M2Y8L5	3-ketoacyl-CoA thiolase	95.85%	PM0083592
61	A0A6M2Y413	Ribose 5-phosphate isomerase B	95.86%	PM0084032
62	A0A6M2Y7D8	Carbamate kinase	95.94%	PM0083630
63	A0A6M2Y993	Cysteine--tRNA ligase	95.94%	PM0083552
64	A0A6S6I272	Glycerol-3-phosphate cytidylyltransferase	95.95%	PM0084041
65	A0A6M2Y4X0	Glycerol kinase	95.97%	PM0084044
66	A0A6M2Y106	Proline--tRNA ligase	95.97%	PM0083676
67	W8R6R8	Fructose-bisphosphate aldolase class-II	95.98%	PM0083991
68	A0A6M2Y185	ATP synthase subunit alpha	95.99%	PM0083554
69	A0A6M2Y4V9	CTP synthase	95.99%	PM0083628
70	A0A6M2Y7P8	Thioredoxin reductase	96.07%	PM0084038
71	A0A6M2Y210	Galactokinase	96.08%	PM0083992
72	A0A6M2Y8Z6	Glycine/betaine ABC transporter	96.11%	PM0084047
73	A0A6M2Y7K8	Hemolysin	96.12%	PM0084049
74	A0A6M2Y8C1	Nucleoside 2-deoxyribosyltransferase	96.15%	PM0083568
75	A0A6M2Y7P1	Geranyltranstransferase	96.17%	PM0083993
76	A0A6M2Y668	GTPase Obg	96.22%	PM0084050
77	A0A6M2Y5Y3	tRNA (guanine-N(1)-)-methyltransferase	96.22%	PM0084043

78	A0A6M2Y065	ATP synthase subunit c	96.29%	PM0083553
79	A0A6M2XZU6	ATP synthase subunit beta	96.30%	PM0083551
80	A0A6M2Y2C2	Proline iminopeptidase	96.30%	PM0083675
81	A0A6M2Y680	Acetate kinase	96.33%	PM0084005
82	A0A6M2XZR3	Dehydrogenase	96.33%	PM0083994
83	A0A4P2VIK8	Aminotransferase	96.34%	PM0084019
84	A0A6M2Y4X6	Cytokinin riboside 5'-monophosphate phosphoribohydrolase	96.39%	PM0084072
85	A0A6M2Y089	Glutamine amidotransferase	96.39%	PM0084052
86	A0A6S6I3E0	dTDP-4-dehydrorhamnose reductase	96.40%	PM0083995
87	A0A6M2Y0L7	Protein-disulfide isomerase	96.43%	PM0083677
88	A0A6M2Y3R4	Glucose-6-phosphate isomerase	96.44%	PM0083996
89	A0A6M2Y2Y7	Cytidine deaminase	96.48%	PM0083997
90	A0A6M2Y8X5	ABC transporter	96.55%	PM0083613
91	A0A6M2Y359	ATPase	96.55%	PM0083634
92	A0A6M2XZ01	DNA gyrase subunit A (EC 5.6.2.2)	96.56%	PM0083998
93	A0A6M2Y3K7	Phosphopantetheine adenylyltransferase	96.56%	PM0083671
94	A0A6M2Y8Q6	Ornithine cyclodeaminase	96.58%	PM0083572
95	A0A6M2Y6E9	Tryptophan--tRNA ligase	96.62%	PM0084045
96	A0A6M2Y4J8	Isopentenyl-diphosphate delta-isomerase	96.63%	PM0084054
97	A0A6M2Y8B1	Aldehyde dehydrogenase	96.66%	PM0084016
98	A0A6M2Y2X1	Cytidylate kinase	96.71%	PM0083999
99	A0A6M2Y2Z7	N-acetylneuraminate lyase	96.75%	PM0084056
100	A0A6M2Y7R3	Acyltransferase	96.77%	PM0084007
101	A0A6M2Y5G8	Aminopeptidase	96.77%	PM0084018
102	A0A6M2Y3V0	Inosine 5'-monophosphate dehydrogenase	96.77%	PM0084058
103	A0A6M2Y155	Putative aspartate ammonia-lyase	96.77%	PM0083678
104	A0A0D5C7M7	Putative transcriptional regulator	96.83%	PM0083580
105	A0A6M2XZB6	Orotate phosphoribosyltransferase	96.84%	PM0083575
106	A0A6M2Y3E5	Probable butyrate kinase	96.85%	PM0083673
107	A0A6M2Y201	Alanine dehydrogenase	96.88%	PM0084015
108	A0A6M2Y8X0	Haloacid dehalogenase	96.89%	PM0084059
109	A0A6M2Y1Q5	Pyrimidine-nucleoside phosphorylase	96.98%	PM0083588
110	A0A6M2Y819	DNA-(apurinic or apyrimidinic site) lyase MutM	97%	PM0084000
111	A0A6M2Y1J5	Adenylosuccinate lyase	97.01%	PM0084011
112	A0A6S6I560	dTDP-4-dehydrorhamnose 3,5-epimerase family protein	97.16%	PM0084001
113	A0A6M2Y8K8	Choline ABC transporter permease	97.35%	PM0083542
114	A0A6M2Y1H6	Nitroreductase family protein	97.41%	PM0083544
115	A0A6M2Y1K7	Holliday junction ATP-dependent DNA helicase RuvB	97.43%	PM0084060
116	A0A6M2Y3L4	NLPA lipoprotein	97.45%	PM0083555
117	A0A6M2XZE7	Peptide methionine sulfoxide reductase MsrA	97.53%	PM0083584
118	A0A6M2Y3Z4	Orotidine 5'-phosphate decarboxylase	97.56%	PM0083698
119	A0A6M2Y007	Cold-shock protein	97.66%	PM0083540
120	A0A6M2Y0V8	Putative N-acetylmannosamine-6-phosphate 2-epimerase	97.69%	PM0083571
121	A0A6M2Y1S2	Diphthine synthase	97.73%	PM0084002
122	A0A6M2Y8Y2	DNA-3-methyladenine glycosylase I	97.77%	PM0084003
123	A0A6M2Y6I0	Guanylate kinase	97.81%	PM0084061
124	A0A6M2Y263	Bacteriocin transporter	97.87%	PM0083538
125	A0A6M2Y727	ABC transporter permease	98.05%	PM0083615
126	A0A6M2Y2Z8	Diacylglycerol kinase	98.31%	PM0084004
127	A0A6M2Y5C2	Recombinase RmuC	98.57%	PM0083601
128	A0A6M2Y274	Adenylate kinase	98.59%	PM0084010
129	A0A6M2Y4T8	Thymidine kinase	98.91%	PM0084040
130	A0A6M2Y1P7	ADP-ribose pyrophosphatase	100%	PM0084013
131	A0A6M2Y634	ATP synthase subunit b	100.00%	PM0083534

Protein-Ligand Docking: The template proteins were selected from PDB website (www.rcsb.org). The template proteins and the proteins of *Erysipelothrix rhusiopathiae* that were modelled in this study were subjected to protein-ligand docking with respective antibiotics that are tabulated in **Table 2**. Results of the docking studies indicate that antibacterial drug Ribostamycin has greater

binding energy of -7.35Kcal/mol with the protein disulphide isomerase of *Erysipelothrix rhusiopathiae* and forms 5 hydrogen bonds with ASP-31, GLU-206, ALA-210, ASN-209 and hydrophobic interactions with ASP-29, LYS30, GLN-211, LYS-212. Ribostamycin with template protein demonstrated lower binding energy of -6.17Kcal/mol and it formed 4 hydrogen bonds with ASP-346, GLU-345, LEU-343, GLU-342, and hydrophobic interactions with GLN-341, ARG-283, and PRO-344, suggesting that Ribostamycin could be used as a potent drug to control swine erysipelas caused by *Erysipelothrix rhusiopathiae*. The graphical representation of protein-ligand interactions between the drug target and the antibiotics is shown in **Fig. 2** and **3**. The list of test antibiotics, template proteins, modelled proteins, and the binding energies are tabulated in **Table 2.**

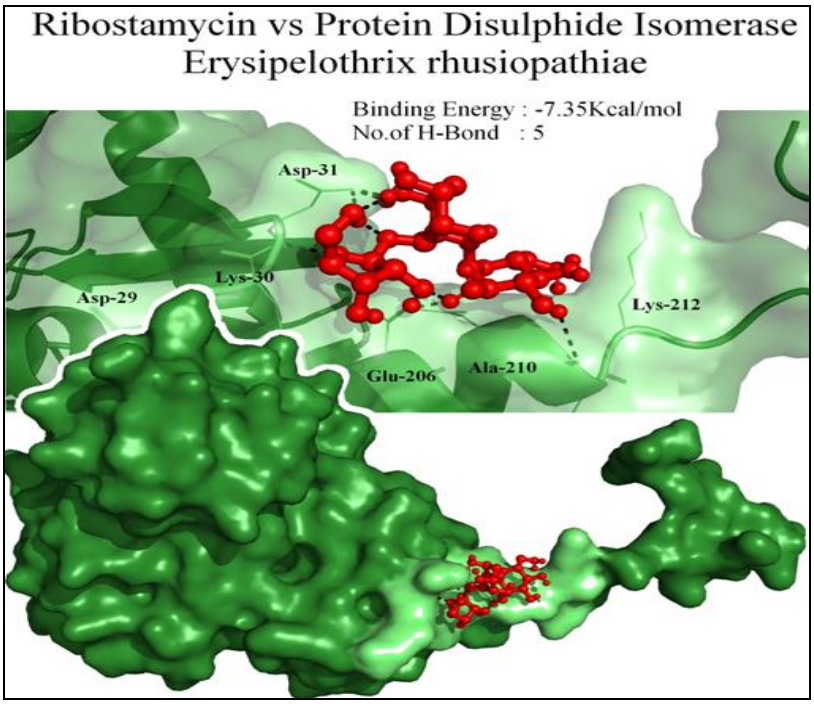

FIG. 2: DOCKING INTERACTION OF ANTIBIOTIC RIBOSTAMYCIN WITH MODELLED

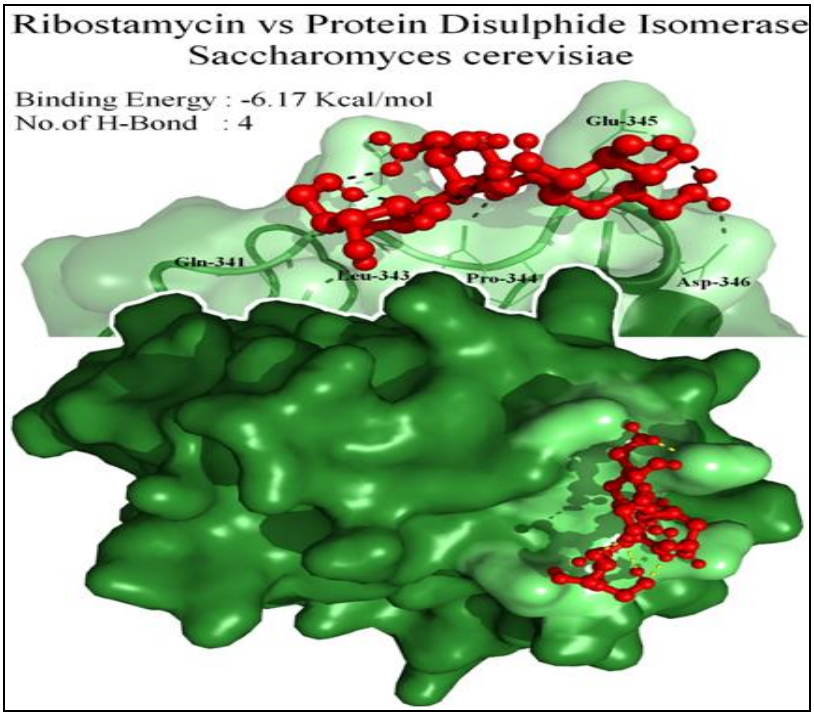

FIG. 3: DOCKING INTERACTION OF ANTIBIOTIC RIBOSTAMYCIN WITH TEMPLATE PROTEINS

TABLE 2: PROTEIN-LIGAND DOCKING ANALYSIS OF HOMOLOGY MODELS AND TEMPLATE PROTEINS WITH STANDARD ANTIBIOTICS

Drug	Drug target	Organisms	Binding Energy
Ribostamycin	Protein Disulphide Isomerase	*Saccharomyces cerevisiae*	-6.17Kcal/mol
		Erysipelothrix rhusiopathiae	-7.35Kcal/mol
Artenimol	Glyceraldehyde-3-phosphate dehydrogenase	*Staphylococcus aureus*	-6.08Kcal/mol
		Erysipelothrix rhusiopathiae	-6.96Kcal/mol
Cycloserine	Alanine racemase	*Escherichia. coli*	-4.47Kcal/mol
		Erysipelothrix rhusiopathiae	-5.49kcal/mol
Pefloxacin	DNA Gyrase subunit A	*Escherichia. coli*	-5.85Kcal/mol
		Erysipelothrix rhusiopathiae	-4.89Kcal/mol
Penicillamine	Putative copper chaperone	*Staphylococcus aureus*	-3.96Kcal/mol
		Erysipelothrix rhusiopathiae	-4.81Kcal/mol
Cefalotin	D-alanyl-D-alanine carboxypeptidase	*Streptomyces sp.R61*	-6.83Kcal/mol
		Erysipelothrix rhusiopathiae	-4.49Kcal/mol

CONCLUSIONS: This study was aimed to construct 3D models of drug targets of *Erysipelothrix rhusiopathiae* that causes swine erysipelas by computational methods.

The 6 modelled proteins and their templates were subjected to docking with 6 different antibiotics.

This analysis suggested that Ribostamycin is a better antibiotic when compared to other antibiotics, which could help curb the infection of *Erysipelothrix rhusiopathiae.* The modeled proteins in this study are accessible to the scientific community in the PMDB database. These structures can be utilized in advanced research using computational methods for drug discovery and design, which aids in hastening the process of *in-vitro* research of this pathogen and thereby improving the economy of the pork sector.

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