Research Article

In silico Comparative Analysis of the Pathogenicity and Molecular Characteristics of Toxic Shock Syndrome Caused by *Staphylococcus aureus* and *Streptococcus pyogenes*

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ABSTRACT

Background: Toxic Shock Syndrome (TSS) is a medical condition caused by *Staphylococcus aureus* and *Streptococcus pyogenes*, affecting T-Cell Receptors (TCRs) and Major Histocompatibility Complex (MHC) in both healthy and immunocompromised individuals. **Aim:** The study identifies the pathogenicity of *S. aureus* and *S. pyogenes* by analyzing the molecular characteristics of the causative proteins in TSS development, TSST-1, or Toxic Shock Syndrome Toxin, in *S. aureus* and the Streptococcal Pyrogenic Exotoxins SpeA and SpeC in *S. pyogenes*. **Materials and Methods:** Through *in silico* analysis, the protein sequences were obtained from the NCBI GenBank and ran for physicochemical profiling with ProtParam and PsortB, the secondary structure determination with PROTEUS2 and Phyre2. Predicted Antigenic Peptide software served to compare the antigenic capacity. Homology modeling through SWISS-MODEL was validated using QMEANDisCo and GMQE scores, then DeepGOWeb for its function identification. **Results:** The analysis revealed SpeA as the most antigenic, with antigen-presenting cells and molecular function in toxin and binding activities. TSST-1 and SpeC also showed antigenicity levels, with TSST-1 being the most antigenic due to its hydrophilic nature. SpeC, with its lowest cellular process and intracellular structure, is primarily deficient in inducing TSS in patients. **Conclusion:** The study's data will aid in the intervention of TSS patients, particularly immunocompromised individuals, benefiting them and public health.

Keywords: Antigenicity, Hydropathicity, Immunocompromised, Toxic Shock Syndrome.

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INTRODUCTION

Staphylococcus aureus, a gram-positive cocci, causes various illnesses including Toxic Shock Syndrome (TSS). Along with *Streptococcus pyogenes*, it is prevalent in both community and hospital settings and is transmitted easily via direct contact and fomites. A 15% carrier rate for *S. aureus* was reported, primarily in the anterior nares, targeting hyaluronic acid.[1] *S. pyogenes*, a catalase and oxidase-negative bacterium, prefers environments with 5% to 10% carbon dioxide and colonize the mouth, anus, and vaginal mucosa, making crowded places key locations for transmission. In the United States, 15% to 30% of children and 5% to 20% of adults suffer from pharyngitis caused by these pathogens, necessitating further investigation into their spread and impact.[2]

S. aureus and *S. pyogenes* cause TSS, an acute-onset sickness, by producing toxins that lead to symptoms including fever, rash, and end-organ damage.[3] Toxins, such as the Toxic Shock Syndrome Toxin 1 (TSST-1) from *S.*

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aureus — Streptococcal Pyrogenic Exotoxins A (SpeA) and C (SpeC) from *S. pyogenes*, act as superantigens and cause cytotoxicity.[4] Earlier studies have established that TSST-1 is the most effective protein from *S. aureus* in inducing TSS. TSST-1 triggers nonspecific interactions between T-cell and MHC-II receptors on Antigen-Presenting Cells (APC), fostering the proliferation of CD4+ and CD8+ T cells.[5] Moreover, existing literature has explored numerous proteins from *S. pyogenes* to cause TSS but SpeA and SpeC appear the most significant. For instance, SpeC was significantly linked to 93% of invasive infections, while SpeA accounts for 62%.[6]

Although organisms of different genera produce these antigenic proteins, they pose similar clinical manifestations to the human body. Superantigens reroute T-cell activation, excessively activating inflammatory cells and cytokines, thus enhancing the immune response against pathogens.[7] Superantigen exposure can significantly increase T-cell proliferation compared to a typical adaptive immune response.[8,9] Hence, understanding the molecular makeup and characteristics of these antigens is crucial for assessing their ability to induce immunologic reactions.

This research employs *in silico* analysis to compare the molecular and functional properties of proteins produced by *S. aureus* and *S. pyogenes*, utilizing bioinformatics tools and online databases such as protein databases.[10] Various parameters can be predicted, including amino acid sequence, molecular mass, hydropathicity, and heterogeneity.[11] Additionally, tools used to study the tertiary structures of proteins reveal relationships between secondary structures.[12] By *in silico* method, the study tests the hypothesis of significant variability in the molecular properties and pathogenicity of TSS caused by *S. aureus* and *S. pyogenes*. This analysis provides insights into the distinct functionalities of TSS-causing proteins, offering valuable information for further research and treatment development in molecular biology.

MATERIALS AND METHODS

Protein Sequence Retrieval and Alignment

The protein sequences of toxins causing TSS from *S. aureus* and *S. pyogenes* were gathered from the NCBI-National Center for Biotechnology Information GenBank in FASTA format for molecular characterization. The selected sequences involved in the pathogenicity of TSS are P06886 (TSST-1) for *S. aureus* and WP_136303595.1 and AMY97736.1 (SpeA and SpeC, respectively) for *S. pyogenes*. The sequences obtained were confirmed and aligned using the UniProt Align tool, determining the percent identity matrix of the proteins to present the conserved regions and percentage of functional similarity.

Profiling of Physicochemical Properties

The FASTA sequences obtained serve to determine the properties of the proteins, such as the Grand Average of Hydropathicity (GRAVY), estimated half-life, N-terminal domain, and instability index, using the ProtParam tool (https://web.expasy.org/protparam/). The PSortB tool (https://www.psort.org/psortb/) was utilized to predict the subcellular localization of the proteins. The Predicted Antigenic Peptide software (http://imed.med.ucm.es/Tools/antigenic.pl) was used to compare antigenic capacity. Using the semi-empirical method of Kolaskar and Tongaonkar, antigenic peptides were determined, thus detecting the frequency of cysteine, valine, and leucine amino acid residues.[13]

Analysis and Modeling of Protein Structure

For protein secondary structure prediction, PROTEUS2 (http://www.proteus2.ca/proteus2/) and Phyre2 (http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index) were used. These tools have a consistent average accuracy of 78% to 89% and can facilitate robust protein structure prediction. The structure homology models of TSST-1, SpeA, and SpeC were generated using the Swiss-Model Bioinformatics Resource Portal's ExPASY Protparam Tool (https://swissmodel.expasy.org/interactive), allowing visualization of different protein domains, and validated using the SWISS-MODEL workspace QMEAN6 program. Using the structural information of the respective proteins, I-TASSER (https://zhanggroup.org/I-TASSER/) was used to compute the Gene Ontology and molecular functions of the TSST-1, SpeA, and SpeC. To add on molecular function prediction, the DeepGOWeb server (https://deepgo.cbrc.kaust.edu.sa/deepgo/) was used.

RESULTS

Protein sequence retrieval and alignment

TSST-1, SpeA, and SpeC protein sequences were retrieved from NCBI GenBank and aligned using the UniProt Align tool, revealing conserved regions of amino acid sequence through the Percent Identity Index (PMI). SpeA and SpeC showed the highest PMI (27.51%), followed by TSST-1 and SpeA (23.61%) and TSST-1 and SpeC (19.23%). The PMI value indicates functional similarity among these proteins. Despite

Table 1: Proteomics of TSST-1, SpeA, and SpeC.

Sl. No.	Properties	TSST-1	SpeA	SpeC
1	Number of Amino Acids	234	251	235
2	Molecular Weight	26,305.89 kDa	29,268.32 kDa	27,372.19 kDa
3	Formula	$C_{1182}H_{1868}N_{304}O_{365}S_4$	$C_{1329}H_{2045}N_{331}O_{397}S_8$	$C_{1241}H_{1931}N_{317}O_{370}S_5$
4	Total No. of Atoms	3,723	4,110	3,864
5	Estimated half-life	30 hr (mammalian reticulocytes, *in vitro*). >20 hr (yeast, *in vivo*). >10 hr (*Escherichia coli*, *in vivo*).	30 hr (mammalian reticulocytes, *in vitro*). >20 hr (yeast, *in vivo*). >10 hr (*Escherichia coli*, *in vivo*).	30 hr (mammalian reticulocytes, *in vitro*). >20 hr (yeast, *in vivo*). >10 hr (*Escherichia coli*, *in vivo*).
6	Instability index	34.12 (stable)	37.36 (stable)	34.16 (stable)
7	Grand Average of hydropathicity (GRAVY).	-0.529	-0.505	-0.464
8	N-terminal sequence	Methionine (M, Met)	Methionine (M, Met)	Methionine (M, Met)
9			Localization scores	
	Cell wall	0.00	0.00	0.00
	Cytoplasmic	0.00	0.00	0.00
	Extracellular	10.0	10.0	10.0
	Final Prediction.	10.00 Extracellular	10.00 Extracellular	10.00 Extracellular

lacking a reference range for highly conserved proteins, the data supports functional commonality in TSS.

Profiling of physicochemical properties

The ProtParam tool provides the GRAVY scores for TSST-1, SpeA, and SpeC: -0.529, -0.505, and -0.464, respectively (Table 1). A negative GRAVY index indicates a protein is hydrophilic and a positive grade for hydrophobic.[14] Hydrophilic proteins can directly manipulate TCRs, contributing to the TSS development, while hydrophobic lack the mechanism. Moreover, the tool provided the molecular weight of each protein: with SpeA being the highest acquiring 26,305.89 kDa, followed by SpeC with 27,372.19 kDa, and TSST-1 with 26,305.89 kDa. Higher molecular weight suggests greater antigenicity, indicating which proteins are more effective in inducing TSS.

Subsequently, PSORTB was used for the determination of protein localization. The result showed that all proteins have a localization score of 10, making them extracellular. The antigenic determinants were identified using the Predicted Antigenic Peptide tool. TSST-1 and SpeC showed eight antigenic determinants, the highest, while SpeA had six. TSST-1, SpeA, and SpeC present with 1.0059, 1.0312, and 1.0173 propensity scores respectively. Antigenic determinants are APC recognition sites while antigenic propensity represents protein antigenic activity.

Analysis and modeling of protein structure

Structural Characteristics

The Protparam tool shows in Figures 1a, 1b, and 1c, that methionine is the N-terminal domain of TSST-1, SpeA, and SpeC that contributes to the proteins' antigenic mechanism.

Moreover, presented in Table 2, the secondary structure was analyzed using PROTEUS2, which showed that TSST-1 has 44 alpha-helices and 81 beta-strands. On the other hand, SpeA and SpeC have 42 alpha-helices but differ in beta-strands, with 105 and 93 residues, respectively. For Phyre2, the model predicted 191 residues for TSST-1, 221 for SpeA, and 200 for SpeC, all with 100.0% confidence for helices and strands. These findings showed that proteins with higher alpha-helix content, like TSST-1, might have a greater potential to induce TSS.[15]

For structure validation, the Swiss Model's Global Model Quality Estimate (GMQE) score, ranging from 0 to 1, assesses the reliability of predicted protein models, with higher scores indicating better model quality.[16,17] For post-modeling assessment, an average per-residue score with an estimated error is represented by the QMEANDisCo score, which is considered ground truth for model quality.[18] The choice of models, influenced by careful consideration for the confidence and accuracy through GMQE and QMEANDisCo scores in Table 3,

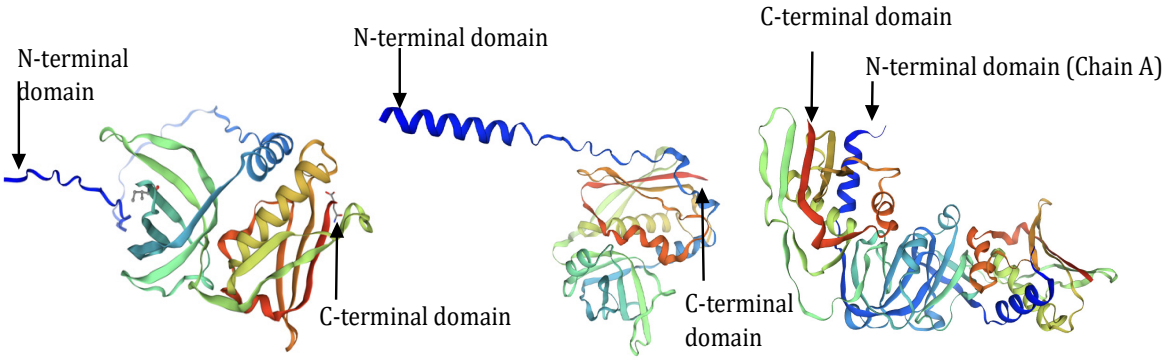

Figure 1a. Tertiary structure of TSST-1 (SWISSMODEL)

Figure 1b. Tertiary structure of SpeA (SWISSMODEL)

Figure 1c. Tertiary structure of SpeC (SWISSMODEL)

Figure 1: The 3D models of TSST-1, SpeA, and SpeC [1a, 1b, and 1c], are colored along their length from the N-terminal to the C-terminal, starting with a blue hue (N-terminal) and ending with a red hue (C-terminal). This facilitates the visualization of secondary structural features such as coils, β-strands, and α-helices.

Table 2: Summary of secondary structure using Phyre2 and PROTEUS 2.

	Phyre 2	PROTEUS 2	Phyre 2	PROTEUS 2	Phyre 2	PROTEUS 2
Protein	**Alpha helices**		**Beta helices**		**Coil content**	
TSST-1	19%	19% (44 residues)	32%	35% (81 residues)		47% (109 residues)
SpeA	16%	17% (42 residues)	38%	42% (105 residues)		41% (104 residues)
SpeC	12%	18% (42 residues)	43%	40% (93 residues)		43% (100 residues)

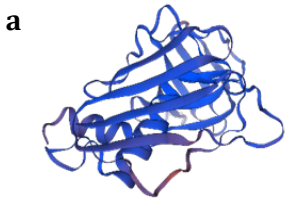

Figure 2a: Model 1 of TSST-1

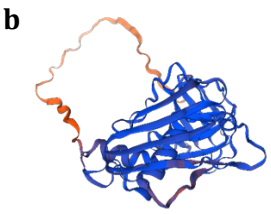

Figure 2b: Model 2 of TSST-1

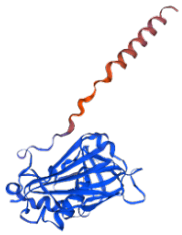

Figure 2c: Model 1 of Exotoxin A

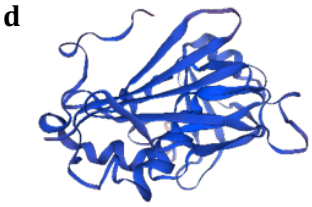

Figure 2d: Model 2 of Exotoxin A

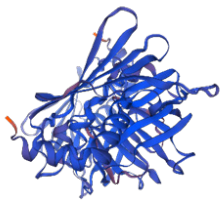

Figure 2e: Model 1 of Exotoxin C

Figure 2: Models 1 and 2 of TSST-1 [2a and 2b]. Models 1 and 2 of Exotoxin A [2c and 2d]. Model 1 of Exotoxin C [2e]. The confidence level is indicated by a gradient, ranging from dark orange (low confidence) to deep blue (high confidence).

Table 3: Tabulated GMQE and QMEANDisCo scores of modeling structures.

Model	GMQE	QMEANDisCo
TSST-1	0.86	-
TSST-1	0.80	0.88±0.06
Exotoxin A	0.90	-
Exotoxin A	0.83	0.90±0.06
Exotoxin C	0.84	0.89±0.05

Functional Characteristics of the Proteins

The DeepGOWeb server identified the functional characteristics of the proteins. Table 4 presents that only TSST-1 is associated with functional organelles or cellular components. SpeA exhibited the most significant molecular functions, particularly in binding and activity, indicating its major role in antigenic and biological processes. For cellular processes, SpeA had the highest score (0.320), followed by TSST-1 (0.317) and SpeC (0.311), reflecting their functional activity within the cell. These findings highlight the mechanisms by which each protein induces TSS.

This table displays the data on the functional characteristics of the proteins according to the DeepGOWeb server. Each row represents the cellular components, molecular functions, and biological processes of the proteins TSST-1, SpeA, and SpeC which correspond to each column. This table should be reproduced at column width.

DISCUSSION

The results highlight the molecular similarities and differences of the three target proteins. By PMI values, SpeA and SpeC are the most functionally similar. All three proteins feature methionine as their N-terminal domain and all are localized extracellularly, implying substantial antigenic potential. Moreover, the hydrophilicity based on the GRAVY score suggests that TSST-1 is the most antigenic. TSST-1 and SpeC exhibit more antigenic determinants. However, SpeA has a higher antigenic propensity score. Finally, DeepGOWeb highlighted SpeA's crucial abilities in binding and activity for antigenic interactions and biological processes.

This study uses *in silico* methods to analyze extensive protein sequences linked to TSS, avoiding live subjects for ethical and cost concerns. Comprehensive tools offer deep insights into structure, function, and attributes, but accuracy hinges on *in silico* data validity. Clinical validation is needed for practical use and generalizability may be limited. Time and resource constraints also influenced the study's scope.

Table 4: Cellular components, molecular function, and biological processes of the three proteins.

	TSST-1 (P06886)	SpeA (WP_136303595.1)	SpeC (AMY97736.1)
Cellular Components			
Cellular Anatomical Entity	0.401	0.376	0.365
Intracellular Anatomical Structure	0.343	0.319	0.330
Organelle	0.331	-	-
Membrane	0.328	-	-
Intracellular Organelle	0.325	-	-
Membrane-Bounded Organelle	0.314	-	-
Intracellular Membrane-Bounded Organelle	0.309	-	-
Molecular Function			
Toxin Activity	-	0.500	-
Binding	-	0.472	-
Protein Binding	-	0.412	-
Signaling Receptor Binding	-	0.338	-
MHC Protein Binding	-	0.323	-
MHC Class II Protein Binding	-	0.323	-
Biological Processes			
Cellular Process	0.317	0.320	0.311
Biological Process Involved in Interspecies Interaction Between Organisms	-	0.544	-
Modulation Process of Another Organism	-	0.506	-

Profiling of physicochemical properties

The amount of TSST-1, SpeA, and SpeC amino acids is 234, 251, and 235, respectively—all within a similar sequence. Other molecular characteristics of the proteins, such as molecular weight and estimated half-life are presented in Table 1.

Hydropathicity is significant in protein antigenicity. Hydrophilic proteins can form hydrogen bonds, ion pairs, and localization on cell surfaces for direct interaction with host receptors.[19] In correlation, a recent study links antigen manipulation of TCRs and MHC-II molecules to impaired cytokine release coordination, contributing to TSS.[20] Considering the values, TSST-1 exhibits the lowest negative hydropathicity score among the studied proteins, indicating high hydrophilicity, followed by SpeA and SpeC. Compared with the study of Kolla *et al.*,[21] their result showed a GRAVY score of -0.458 for TSST-1. Although it is lower compared to the researchers' data, the hydrophilicity is similar, and the significant antigenicity of the protein has been noted. Thus, TSST-1 is the most antigenic in terms of hydropathicity.

Moreover, the molecular weight can directly influence antigenicity.[22] An antigen or immunogen must have 10,000 Da on its molecular weight for immune system recognition and response. TSST-1, SpeA, and SpeC exceed 100,000 Da. With the large size of the proteins, they are insoluble, and easily processed and ingested by macrophages for lymphocyte presentation.[22]

Antigenicity of TSST-1, SpeA, and SpeC

TSST-1 and SpeC have higher antigenic determinants than SpeA. However, SpeA presents a higher average antigenic propensity than SpeC and TSST-1. A greater amount of epitopes means greater recognition and binding sites for T-cells.[23] Meanwhile, a higher propensity score reflects a higher tendency of antigenic activity in the identified antigenic determinants. Under Kolaskar and Tongaonkar's method, SpeA possesses the most Cys, Leu, and Val residues.

Furthermore, zinc-dependent superantigens form a more stable complex with higher binding affinity with MHC class II on APCs.[9] SpeC utilizes the polymorphic HLA-DR β-chain and has a higher antigenicity score than TSST-1 due to its high-affinity and Zn-dependent binding site on MHC class II. TSST-1 is selective to the α-chain of HLA-DR due to the absence of the Zn atom at the C-terminal of the β chain.[24]

Unlike TSST-1 and SpeC, SpeA almost exclusively binds with HLA-DQ. SpeA induces a significantly higher amount of TNF-α-, TNF-β-, IL-2, and IFN-γ when presented by HLA-DQ rather than HLA-DR.[25] Also, certain strains of SpeA have been found to possess zinc-binding sites that help stabilize antigen-MHC complexes.[26,27] The binding behavior of SpeA supports its higher antigenicity score than that of TSST-1 and SpeC. Although the SpeC superantigen gene was substantially isolated in 93% of invasive S. pyogenes strains, 38% of non-invasive infections were attributed to SpeA.[6] Nonetheless, despite having slightly greater amounts of antigenic determinants, TSST-1 and SpeC are likely to induce TSS with lesser intensity than SpeA.

Localization of Proteins

The predicted subcellular localization of TSST-1, SpeA, and SpeC is extracellular, demonstrating the existence of a signal peptide. A localization score greater than 7.5 indicates final localization prediction. A protein's subcellular localization is linked to its role in an organism's biological function.[28] Extracellular proteins primarily interact with their external environment, involving processes like signaling immune response.

Exotoxins are highly antigenic proteins composed of subunit A, which is responsible for enzymatic activities that modify intracellular proteins, and subunit B, which targets the host cell to facilitate the interaction between subunit A and the molecular target. Their pathogenicity is attributed to their enzymatic activities, including their virulence factor.[29]

Analysis and modeling of protein structure

N-terminal Domain of TSST-1, SpeA, and SpeC

The Protparam tool identified methionine as the N-terminus of all three target sequences. The hydrophobic stop codon has antioxidant properties, preventing protein degradation. However, it is susceptible to oxidation to methionine sulfoxide, affecting its antigenicity and protein stability.[30] Crystallography of superantigens reveals that residues responsible for interacting with MHC-II molecules are located within the N-terminal domain.[9,31] Hence, this property is linked with numerous disease processes and could promote optimized expression of the TSS-inducing proteins.

Analysis of Secondary Structure of TSST-1, SpeA, and SpeC

Table 2 shows β-strand and α-helix content analyzed by PROTEUS2 and Phyre2. Both software demonstrated a predominance of β-strands over α-helices, with the α-helices percentages closely grouped. PROTEUS2 revealed that TSST-1 has 19% alpha-helices, whereas SpeA and SpeC have 17% and 18%, respectively. Conversely, Phyre2 revealed that TSST-1 and SpeA share similar α-helix content at 16%, while SpeC has

12%. Protein regions with higher α-helix content are more likely to cause diseases.[15] Therefore, TSST-1 and SpeA may have a greater potential to induce TSS.

Protein Rigidity and Functional Variability in TSST-1, SpeA, and SpeC

Normalized B-Factor Profiles (BFPs) assess atom, side chain, or region rigidity from thermal motion in proteins.[32] I-TASSER analysis showed that N- and C-terminal regions and most loops have positive or near-zero normalized B-factors, indicating a more ordered protein structure.[33] Accordingly, TSST-1, SpeA, and SpeC are well-ordered structures that tend to be more rigid and stable, unlike disordered structures with high B-factor involved in tissue-specific interactions and can be alternatively spliced.[34] The result shows consistency with the instability index prediction presented in Table 1.

The SpeA protein was also predicted to be associated with metal ion binding (GO:0046872). Metal ion binding sites enhance the stability and biological activities of proteins.[35] SpeA's metal ion binding ability may impact its stability and interactions with host cells, potentially influencing the pathogenicity of *S. aureus* and *S. pyogenes* associated with TSS.

In another aspect, the study utilized the DeepGOWeb server to predict the functions of three proteins, revealing significant differences. Presented in Table 4, the TSST-1 protein is a significant cellular entity, created by a cellular organism with granularity exceeding the protein complex's level.[36] It also has other components that SpeA and SpeC proteins lack, including organelle, membrane, intracellular organelle, etc.

SpeA, with a toxin activity of 0.500, is highly functional on molecular function, with compounds potentially concerning immune-compromised individuals. It has multiple binding functions, including the MHC and MHC II-essential for immune response coordination and T-cell recognition.[37] SpeA's efficient binding to hosts surpasses that of TSST-1 and SpeC, indicating its potential for invulnerability and effectiveness in prompting host immune responses.

Regarding biological processes, SpeA protein is the most effective, involving cellular processes and interspecies interactions, which can be beneficial or harmful depending on an individual's immunological abilities.[38] It also has a modulation process, allowing it to adapt to a new environment, such as the human body.[39] However, an *in vivo* study found that, unlike SpeA, TSST-1 uniquely crosses epithelial cell membranes to induce TSS, evidenced by the death of test rabbits after oral and vaginal administration of the toxins. SpeA did not cause toxicity through these routes, suggesting TSST-1's more effective adaptability. Nonetheless, the study noted that SpeA is a more potent superantigen, remarkably when acquired subcutaneously.[40]

In light of the findings discussed, TSST-1, SpeA, and SpeC have significant implications for health practice and research. Profiling these proteins enhances understanding of their antigenicity and immune interactions, aiding the advancement of targeted therapeutics for TSS. The study supports developing hydrophilic medications that can interfere with the attachment of bacteria to host T-cells, thus alleviating adverse clinical effects. In addition, the data collected outlines a firm basis for *in vivo* and *in vitro* investigations, stimulating further analysis of the molecular mechanisms driving TSS. Genetic sequence databases have strengthened these findings and can be employed to evaluate other superantigens and associated pathogens. These findings, while promising, require application in actual TSS cases, encouraging further examination to extend the field of study and applications.

CONCLUSION

This study examined the molecular characteristics and pathogenic roles of TSST-1 from *S. aureus* and SpeA and SpeC from *S. pyogenes*, focusing on their structures, biological mechanisms, and contributions to TSS. SpeA showed stronger antigenicity than TSST-1 and SpeC due to its binding to MHC molecules and TCRs, influenced by size, structure, and other features. Protein traits affect TSS potential, but individual immune status is also essential. These findings aid *in vivo* and *in vitro* studies for better treatment and management. *In silico* methods help predict protein mechanisms relevant to pathogenicity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

APCs: Antigen-Presenting Cells; **GMQE:** Global Model Quality Estimate; **GRAVY:** Grand average of hydropathicity index; **MHC:** Major Histocompatibility

Complex; **NCBI:** National Center for Biotechnology Information; **PMI:** Percent Identity Index; ***S. aureus*:** *Staphylococcus aureus*; ***S. pyogenes*:** *Streptococcus pyogenes*; **SpeA:** Streptococcal Pyrogenic Toxins A, **SpeC:** Streptococcal Pyrogenic Toxins C; **TSS:** Toxic Shock Syndrome; **TCRs:** T-cell receptors; **TSST-1:** Toxic Shock Syndrome Toxin-1.

SUMMARY

Toxic Shock Syndrome (TSS), caused by *S. aureus* and *S. pyogenes*, affects T-cell receptors and Major Histocompatibility Complex (MHC) triggering symptoms like fever, rash, and end-organ damage. TSST-1 from *S. aureus* and SpeA and SpeC from *S. pyogenes* are key proteins implicated in causing TSS. Using NCBI and web tools (ProtParam, PROTEUS2, PSortB, DeepGOWeb, I-TASSER, PHYRE2, SWISS-MODEL), their sequences-TSST-1 (P06886), SpeA (WP_136303595.1), and SpeC (AMY97736.1)- and structures were analyzed for their capacity to influence one's immune system. Before analyzing the proteins, the sequence, secondary, and tertiary structures were validated, showing high confidence and conserved region for accuracy and functional similarities. The analysis highlighted SpeA as the most antigenic and TSS-causing. This is due to its high antigenic propensity associated with antigenic activity, having the most molecular function, particularly in toxin activity, T-cell binding and MHC binding, and biological processes. Although TSST-1 and SpeC also demonstrated antigenicity due to their molecular weight, hydrophilic hydropathy, extracellular antigenic activity, and antigenic determinants, their intensity was comparatively lesser. The immune system's significant role in managing these proteins in the context of TSS underscores the importance of further understanding these molecular mechanisms.

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