Brief Report

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Marine-derived Plastic-binding Peptides

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Abstract

Peptides can be used as reagents in enzyme-linked immunosorbent assays (ELISA), in which the sample is immobilized on a solid support, usually a polystyrene plate. Polystyrene-binding peptides allow site-specific immobilization of proteins or antibodies directly onto polystyrene (PS) plates with minimal conformational change. Additionally, micro- and nanoplastics pose a significant threat to all life forms in the environment, and the development of biosensors for their detection is considered a pressing need in the field. PS is also used as a support in solid-phase peptide synthesis. In this brief report, we analyzed 3505 marine-derived peptides using machine-learning algorithms to introduce novel and putative PS-binding peptides. Seven strong candidates, mainly derived from *Conus* species, were the most optimal PS-binders. PS-binder peptides were cationic or cationic amphipathic, composed of helical structures. π-π stacking, hydrophobic, and electrostatic interactions were involved in the attachment of peptides to plastics. Some PS-binding peptides were identified to be active against pathogenic bacteria, making them promising candidates as biomaterials to prevent medical device-related infections. Taken together, the novel identified peptides are suggested as a capturing reagent on PS surfaces for biomedical applications.

Keywords: Bioactive peptides; Biomaterial; Immobilization; Polystyrene; Solid-phase peptide synthesis.

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1. Introduction

Microplastics, fragmented from everyday human waste, have been recognized as a serious threat to biological systems and the global environment (1-3). The most harmful microplastics are typically smaller than one millimeter in size and have the potential to bind toxic substances that are likely to be mistaken for food by marine animals. Furthermore, nano-sized microplastics or nanoplastics have been reported to pose a significant risk to human health (4,5). In addition to the issues associated with nanoplastic sampling methods, there are also other problems with nanoplastic and microplastic detection systems using fluorescent staining or Raman spectroscopy (6,7). Surface/polymer-binding peptides (SBPs) can efficiently functionalize polymer surfaces offering numerous applications, including the oriented immobilization of catalytic enzymes, antigens, and bioactive peptides. SBPs are applicable in biosensors. Reports describe screening for oligopeptides that can selectively bind to the surfaces of microplastics, such as polystyrene, polyethylene, and polypropylene (8-10). Polystyrene (PS) has long been used as a support for solid-

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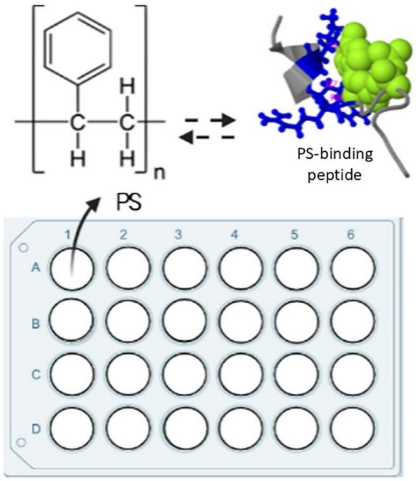

Figure 1. A schematic representation of a polystyrene-plate surface and its interaction with a polystyrene-binding peptide.

phase peptide synthesis (SPPS) (11). PS has been used exclusively as a solid surface for protein immobilization in enzyme-linked immunosorbent assay (ELISA) and animal cell culture. Chemical conjugation of PS-binding peptides with target proteins such as enzymes, antibodies, and streptavidin allows for efficient immobilization of target proteins while maintaining higher biological activity than physically adsorbed proteins (Figure 1). In this brief report, we introduce novel PS-binding tags derived from a library of marine-derived peptides applicable to biomaterials. Antimicrobial characteristics of the identified PS-binding peptides against selected Gram-positive and Gram-negative pathogenic bacteria are also investigated.

2. Materials and Methods

To introduce putative PS-binding peptides, 3505 available bioactive peptides from a library of 82 marine species in our previously published investigation have been screened (12). In this study, PS-binding peptides were identified using the PSBinder tool, considering the SVM algorithm, which is available on the SAROTUP program (13) (Accessed October 2025). This program has a sensitivity, specificity, accuracy, and the Matthews correlation coefficient (MCC) of 88.46%, 85.58%, 87.02%, and 0.74, respectively. PS19-1 (RAFIASRRIRRP), reported by Kumada et al., was used as an experimentally validated positive control. It binds antibodies to a PS fixed plate (14). Conformational and modeling analyses were conducted using the i-TASSER program (15). The helical wheel of amphipathic peptides was analyzed by the HeliQuest program (16). Strain-specific antimicrobial characteristic of PS-binding peptides against bacterial species, including *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae*, and *Staphylococcus aureus* ATCC 25923 was predicted using the DBAASP tool based on ML approaches (17). Annotation of peptides is composed of two sections, which show the peptide length followed by its annotated number in the library. For example, PEP10-963 is a 10-mer PS-binding peptide.

3. Results and Discussion

The development of methods for immobilizing proteins on surfaces is important for the construction of high-throughput protein-based bioassay systems, such as antibody microarrays and micrototal analysis systems. Several immobilization methods have been developed that enable proteins to be attached to various solid supports while maintaining their maximum biological functionality (18). In conventional physical adsorption and chemical coupling methods, protein molecules are often immobilized on the surface in an un-

Table 1. Polystyrene-binding peptides from marine sources, their secondary structure, and physiochemical properties. C-score: confidence score; TM-score: template modeling score.

ID	Seq	Structure	C-score	TM-score	Helix (%)	Coil (%)	Charge	pI	Species
PEP10-963	KNFWKRNLYL	CCCCHH-HCCC	–0.06	0.71±0.12	30	70	3	10.30	*Conus betulinus*
PEP10-1679	KRLANLYLKA	CCCHHHH-HCC	0.09	0.73±0.11	50	50	3	10.30	*Conus pennaceus*
PEP10-1680	RLANLYLKAR	CCCHHHH-HCC	–0.50	0.65±0.13	50	50	3	11.01	*Conus pennaceus*
PEP10-962	LKNFWKRNLY	CCCHHH-HCCC	0.21	0.74±0.11	40	60	3	10.30	*Conus betulinus*
PEP15-101	WCFSTRVVLKM-KQRA	CCCCCCH-HHHHHCCC	–0.76	0.62±0.14	40	60	4	11.02	*Synanceia verrucosa*
PEP15-539	RRSLKNFWKRN-LYLR	CCCCHHH-HHHHHCCC	–0.71	0.62±0.14	53.33	46.67	6	12.02	*Conus betulinus*
PEP15-560	RRSLKDFWKRH-FYLR	CCCCHHH-HHHHHCCC	–0.15	0.69±0.12	53.33	46.67	5.5	11.57	*Conus betulinus*

favorable orientation and are likely to be denatured during the immobilization process. In contrast, site-specific immobilization methods that use affinity peptides for binding appear to effectively preserve biological activity and allow control over the orientation of adsorbed protein molecules (14).

To identify peptides that bind to polystyrene surfaces, we screened 3505 marine-derived bioactive peptides using the PSBinder program. At a threshold of 0.5, a total of 47 peptides were identified as PS-binders. However, only seven peptides with scores higher than 0.9 were submitted for further analysis (Table 1). PS19-1, as the positive control, displayed a score of 0.81. All seven peptides were cationic, with pI values in the range of 10-12. Structurally, all peptides showed a mixture of coil and helical conformations. I-TASSER reliability metrics, such as confidence score (C-score) and template modeling score (TM-score), were in the acceptable range. The C-score (ranging from –5 to +2) quantifies the overall confidence of the predicted model based on threading quality and structural convergence. Higher values indicate more reliable

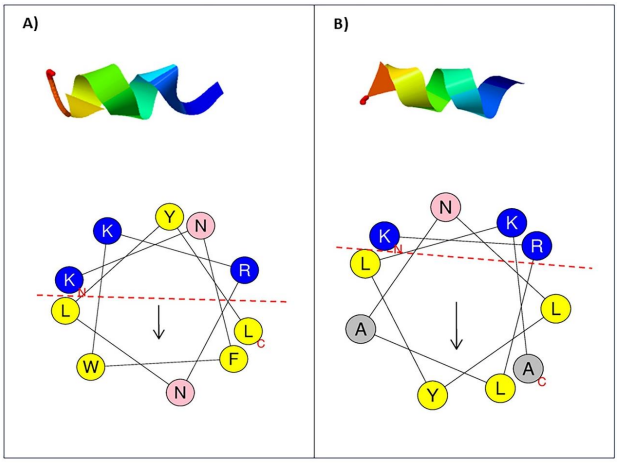

Figure 2. Helical conformation and helical wheel representation of amphipathic peptides A) PEP10-963 and B) PEP10-1617. The red dotted line delineates the spatial segregation between the cationic face of the peptide, composed of K and R residue blue circles, and the hydrophobic face, comprising L, W, and F yellow residues.

predictions. The estimated TM-score (0-1) evaluates how closely the predicted fold is expected to match the true native structure, with scores above 0.5 suggesting a correct global topology (Table 1).

Some peptides, such as PEP10-963 and PEP10-1679, displayed secondary amphipathic structure according to the segregation of the cationic and hydrophobic faces (Figure 2). The presence of Trp, Phe, and Tyr residues in PEP10-962, PEP10-963, PEP15-539, and PEP15-560, which harbor aromatic rings, is responsible for forming π-π stacking interactions with the polystyrene benzene ring (19). The side chain of hydrophobic residues, such as Val and Leu, forms strong hydrophobic interactions with polystyrene. Charged basic residues such as Arg, Lys, and His, as well as Asp, an acidic amino acid residue, can be observed in PS-binding peptides. Charged residues, Asn and Gln, can be ionized at acidic and basic pH environments and bind to the polymer through electrostatic interactions (19). Therefore, the novel identified peptides are suggested for immobilization of catalytic enzymes, antigens, and antibodies in an aqueous environment.

Polystyrene has been the standard substrate for adherent mammalian cell culture for decades because of its optical clarity and amenability to surface treatment (20). Medical-grade PS is a valuable biomaterial to prevent bacterial colonization and medical device-related infections (21). While *E. coli*, *P. aeruginosa*, and *K. pneumoniae* are Gram-negative rod bacteria that cause device-associated and hospital-acquired infections, *S. aureus* is a Gram-positive coccus, a principal cause of surgical-site and implant infections. The Database of Antimicrobial Activity and Structure of Peptides (DBAASP) was used to introduce bifunctional peptides with both PS-binding and antimicrobial characteristics (Table 2). Except for PEP10-962 and PEP10-1680, other candidates were active against both Gram-positive and Gram-negative bacteria. Longer peptides (15-mer) showed broader-spectrum activity than shorter decapeptides, as evidenced by the predicted MIC values lower than 25 µg/ml.

Peptide labelling, adsorption and kinetic analysis, antimicrobial assays, and cytocompatibility testing can be proposed to experimentally validate the in silico results. Peptides should be labelled with FITC using established dye-coupling protocols to enable fluorescence adsorption assays (22). Polystyrene binding and real-time interaction kinetics can then be quantified by quartz crystal microbalance with dissipation (QCM-D) or surface plasmon resonance (SPR) spectroscopy. Surface chemistry can be confirmed by X-ray photoelectron spectroscopy (XPS)

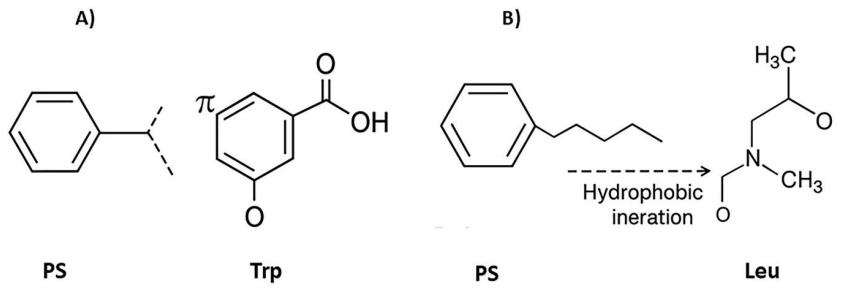

Figure 3. The most significant interactions between polystyrene (PS) and PEP10-962. A) Schematic representation of π–π interactions between the indole ring of tryptophan (Trp) and the aromatic ring of polystyrene B) Schematic depiction of hydrophobic interactions between the leucine (Leu) side chain within the peptide LKNFWKRNLY and the polystyrene surface. On the right, the leucine residue is shown in the context of the peptide backbone, highlighting its isobutyl side chain. A dashed line indicates the proposed hydrophobic interaction between the nonpolar leucine side chain and the hydrophobic polystyrene surface.

Table 2. Strain-specific antimicrobial potency of polystyrene-binding peptides. Active peptides are defined as having an MIC<25 µg/ml.

ID	*E. coli*	*P. aeruginosa*	*K. pneumoniae*	*S. aureus*
PEP10-963	X	√	√	√
PEP10-1679	X	X	√	√
PEP10-1680	X	X	X	X
PEP10-962	X	X	X	X
PEP15-101	√	√	X	√
PEP15-539	√	X	X	√
PEP15-560	√	X	X	√

and contact-angle analysis will be verified for immobilization (23). Antimicrobial activity of peptides can be determined by standard broth microdilution and time-kill assays, such as MIC and MBC. The surface activity can be defined by direct CFU-recovery assays or staining with confocal laser scanning microscopy (24).

4. Conclusion

Developing machine-learning and deep-learning algorithms is now a prerequisite for high-throughput analysis, facilitating efficient wet-lab studies. This report introduced seven highly potent polystyrene-binding peptides that predominantly exhibit helical and cationic structural features. PEP15-101 (WCFSTRVVLKMKQRA), which, besides PS-binding capacity, shows putative antimicrobial potency against resistant pathogenic species, such as *E. coli*, *P. aeruginosa*, and *S. aureus*, is recommended as an optimal candidate to formulate biomaterials used in medical devices. Peptide labelling, adsorption analysis, and antimicrobial assays are required for experimental validation of predictions.

Authors contributions

Conceptualization, S.H.; methodology, S.H.; software, N.N.; validation, S.H. and Z.G.; formal analysis, N.N.; resources, S.H.; writing—original draft preparation, S.H.; writing—review and editing, S.H.; N.N; and Z.G.; supervision, S.H.; project administration, S.H. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Gouin T, Becker RA, Collot AG, Davis JW, Howard B, Inawaka K, *et al*. Toward the development and application of an environmental risk assessment framework for microplastic. *Environ Toxicol Chem.* 2019;38(10):2087-100. doi: 10.1002/etc.4529. Epub 2019 Aug 27. PMID: 31233238; PMCID: PMC6852392.
2. Sharma S, Chatterjee S. Microplastic pollution, a threat to marine ecosystem and human health: a short review. *Environ Sci Pollut Res Int.* 2017;24(27):21530-47. doi: 10.1007/s11356-017-9910-8. Epub 2017 Aug 16. PMID: 28815367.
3. Wu P, Huang J, Zheng Y, Yang Y, Zhang Y, He F, *et al*. Environmental occurrences, fate, and impacts of microplastics. *Ecotoxicol Environ Saf.* 2019;184:109612. doi: 10.1016/j.ecoenv.2019.109612. Epub 2019 Aug 30. PMID: 31476450.
4. Kögel T, Bjorøy Ø, Toto B, Bienfait AM, Sanden M. Micro- and nanoplastic toxicity

on aquatic life: Determining factors. *Sci Total Environ*. 2020;709:136050. doi: 10.1016/j.scitotenv.2019.136050. Epub 2019 Dec 19. PMID: 31887526.
5. Vismara A, Gautieri A. Molecular insights into nanoplastics-peptides binding and their interactions with the lipid membrane. *Biophys Chem*. 2024;308:107213. doi: 10.1016/j.bpc.2024.107213. Epub 2024 Feb 27. PMID: 38428229.
6. Domogalla-Urbansky J, Anger PM, Ferling H, Rager F, Wiesheu AC, Niessner R, *et al*. Raman microspectroscopic identification of microplastic particles in freshwater bivalves (Unio pictorum) exposed to sewage treatment plant effluents under different exposure scenarios. *Environ Sci Pollut Res Int.* 2019;26(2):2007-2012. doi: 10.1007/s11356-018-3609-3. Epub 2018 Nov 20. PMID: 30456620.
7. Schymanski D, Goldbeck C, Humpf HU, Fürst P. Analysis of microplastics in water by micro-Raman spectroscopy: Release of plastic particles from different packaging into mineral water. *Water Res.* 2018;129:154-162. doi: 10.1016/j.watres.2017.11.011. Epub 2017 Nov 6. PMID: 29145085.
8. Hu YF, Gao XC, Xu TQ, Dun Z, Yu XL. Characterization of seven new polystyrene plates binding peptides from a phage-displayed random 12-Peptide library. *Comb Chem High Throughput Screen.* 2016;19(4):283-9. doi: 10.2174/1386207319666160316122106. PMID: 26980286.
9. Rübsam K, Weber L, Jakob F, Schwaneberg U. Directed evolution of polypropylene and polystyrene binding peptides. *Biotechnol Bioeng.* 2018;115(2):321-330. doi: 10.1002/bit.26481. Epub 2017 Nov 15. PMID: 29064564.
10. Vendrell RC, Ajagekar A, Bergman MT, Hall CK, You F. Designing microplastic-binding peptides with a variational quantum circuit-based hybrid quantum-classical approach. *Sci Adv.* 2024;10(51):eadq8492. doi: 10.1126/sciadv.adq8492. Epub 2024 Dec 18. PMID: 39693432; PMCID: PMC11654670.
11. Wang F, Yu L, Li C, Xia X, Zhang F, Linhardt RJ. Site-specific immobilization of papain on DDI-modified polystyrene beads for the oligo (γ-ethyl-L-glutamate) synthesis. *Appl Catal A: Gen*. 2022;630:118472.
12. Hemmati S, Rasekhi Kazerooni H. Polypharmacological cell-penetrating peptides from Venomous marine animals based on immunomodulating, antimicrobial, and anticancer properties. *Mar Drugs.* 2022;20(12):763. doi: 10.3390/md20120763. PMID: 36547910; PMCID: PMC9787916.
13. Li N, Kang J, Jiang L, He B, Lin H, Huang J. PSBinder: A web service for predicting polystyrene surface-binding peptides. *Biomed Res Int.* 2017;2017:5761517. doi: 10.1155/2017/5761517. Epub 2017 Dec 27. PMID: 29445741; PMCID: PMC5763211.
14. Kumada Y, Kuroki D, Yasui H, Ohse T, Kishimoto M. Characterization of polystyrene-binding peptides (PS-tags) for site-specific immobilization of proteins. *J Biosci Bioeng.* 2010;109(6):583-7. doi: 10.1016/j.jbiosc.2009.11.005. Epub 2009 Dec 14. PMID: 20471598.
15. Yang J, Zhang Y. I-TASSER server: new development for protein structure and function predictions. *Nucleic Acids Res.* 2015;43(W1):W174-81. doi: 10.1093/nar/gkv342. Epub 2015 Apr 16. PMID: 25883148; PMCID: PMC4489253.
16. Gautier R, Douguet D, Antonny B, Drin G. HELIQUEST: a web server to screen sequences with specific alpha-helical properties. *Bioinformatics.* 2008;24(18):2101-2. doi: 10.1093/bioinformatics/btn392. Epub 2008 Jul 28. PMID: 18662927.
17. Vishnepolsky B, Grigolava M, Managadze G, Gabrielian A, Rosenthal A, Hurt DE, *et al*. Comparative analysis of machine learning algorithms on the microbial strain-specific AMP prediction. *Brief Bioinform.* 2022;23(4):bbac233. doi: 10.1093/bib/bbac233. PMID: 35724561; PMCID: PMC9294419.
18. Laycock BG, Chan CM, Halley PJ. A review of computational approaches used in the modelling, design, and manufacturing of biodegradable and biobased polymers. *Prog Polym Sci.* 2024;157:101874.

19. Qiang X, Sun K, Xing L, Xu Y, Wang H, Zhou Z, et al. Discovery of a polystyrene binding peptide isolated from phage display library and its application in peptide immobilization. *Sci Rep*. 2017;7(1):2673.
20. Lerman MJ, Lembong J, Muramoto S, Gillen G, Fisher JP. The evolution of polystyrene as a cell culture material. *Tissue Eng Part B Rev*. 2018;24(5):359-72. doi: 10.1089/ten.TEB.2018.0056. PMID: 29631491; PMCID: PMC6199621.
21. Negut I, Bita B, Groza A. Polymeric coatings and antimicrobial peptides as efficient systems for treating implantable medical devices associated-infections. *Polymers (Basel)*. 2022;14(8):1611. doi: 10.3390/polym14081611. PMID: 35458361; PMCID: PMC9024559.
22. Hintzen JCJ, Devrani S, Carrod AJ, Bayik MB, Tietze D, Tietze AA. Fluorescence labeling of peptides: Finding the optimal protocol for coupling various dyes to ATCUN-like structures. *ACS Org Inorg Au*. 2024;4(5):517-525. doi: 10.1021/acsorginorgau.4c00030. PMID: 39371321; PMCID: PMC11450724.
23. Redondo-Gómez C, Parreira P, Martins MCL, Azevedo HS. Peptide-based self-assembled monolayers (SAMs): what peptides can do for SAMs and vice versa. *Chem Soc Rev*. 2024;53(8):3714-73.
24. Lu Z, Liang X, Deng W, Liu Q, Wang Y, Liu M, *et al*. Studies on the antibacterial activity of the antimicrobial peptide Mastoparan X against methicillin-resistant Staphylococcus aureus. *Front Cell Infect Microbiol*. 2025;15:1552872. doi: 10.3389/fcimb.2025.1552872. PMID: 40510797; PMCID: PMC12159006.