Proceedings of Anticancer Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/PAR
ISSN Online: 2208-3553
ISSN Print: 2208-3545

In Silico Evaluation of Potential Ligands of Cancer Cells for Surfactin from *Bacillus* spp.

Mahmuda Akhter Akhi[1], Umme Tamanna Ferdous[2], Md. Fakruddin[3], Suvamoy Datta[1], Md. Asaduzzaman Shishir[1]*

[1]Department of Microbiology, Primeasia University, Banani, Dhaka-1213, Bangladesh

[2]Aquatic Animal Health and Therapeutics Laboratory (Aqua Health), Institute of Bioscience, Universiti Putra Malaysia, Serdang 43400, Selangor, Malaysia

[3]Department of Biochemistry and Microbiology, North South University, Bashundhara, Dhaka-1229, Bangladesh

***Corresponding author:** Md. Asaduzzaman Shishir, md.shishir@primeasia.edu.bd

Copyright: © 2023 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Cancer is one of the most prevalent diseases worldwide, which causes significant morbidity and mortality. Designing and developing a potential anti-cancer drug is an active field of research worldwide. Microorganisms have been considered a potential source of anti-cancer drugs. One such microbe-derived compound is surfactin, which shows potential anti-cancer activities. In this study, we evaluated the binding potential of surfactin with several cancer cell ligands via an *in-silico* approach. Hence, molecular docking studies were performed to test the binding potential of surfactin against four targets. The analyses revealed that surfactin from *Bacillus* sp. can bind with the targeted ligands (coenzyme A, D-leucine, glycerol, and (R)-3-hydroxytetradecanal) with significant affinity. Surfactin showed the highest binding affinity (-7.7 kcal mol^{-1}) to coenzyme A among the targeted ligands. These results may be useful for developing anti-cancer drugs. Nevertheless, further experimental studies are needed to investigate the ligand binding capacity and anti-cancer potential of such surfactin-like molecules.

Keywords: Molecular docking; Cancer; Ligand; Surfactin; *Bacillus*

Online publication: May 29, 2023

1. Introduction

Cancer may develop when cells in one part of the body grow and reproduce uncontrollably. Cancerous cells can invade healthy tissue, including organs and then wreak havoc. Males are more likely to develop cancer of the prostate, lung, colon, and urinary bladder, whereas females are more likely to develop cancer of the breast, lung, colon, uterine corpus, and thyroid gland [1-3]. Cancer treatment with anticancer drugs is costly and can result in cell mutations, thus making them resistant to anticancer drug therapy [1,4]. Numerous studies are being conducted to identify potential anticancer drugs with comparable efficacy. Several studies have suggested that bacteria-derived therapeutic agents are effective in the treatment of cancer [5-7].

Certain specific tumor-targeting bacterial bioactive metabolites have demonstrated impressive efficacy in cancer treatment [8]. Surfactin, iturin, bacillomycin D, and fengycin are well known for their potent anticancer action against various cancer cell lines [9,10]. Surfactin, a cyclic lipopeptide that is also a bacteria-derived biosurfactant, has been demonstrated to elicit cytotoxicity against various malignancies [11]. It has been reported that surfactin has cytotoxic effect on several human cancer cell lines but lower toxicity to normal human fibroblast cells [12]. Other studies have reported similar findings, with surfactin exhibiting a

greater degree of toxicity toward cancer cells compared to normal cells.

Bacillus subtilis, *Bacillus amyloliquefaciens*, and *Bacillus velezensis* are the primary bacterial sources of lipopeptides, including surfactin [11]. These bacteria are safe, renowned for various biological activities, available in nature, and simple to isolate, cultivate, and manipulate in laboratories [13-15]. In their use as alternatives for the treatment of various cancers, more research is needed to fully understand the potential of surfactin and its mode of action.

Surfactin, among other lipopeptides, has a generalized effect and significantly benefits from its ability to penetrate the cell membranes of both gram-positive and gram-negative bacteria. It has both hydrophilic (water-loving) and hydrophobic (water-fearing) properties that keep it stable in both conditions and allow its interaction with cell membranes, which also have hydrophilic and hydrophobic regions. Several mechanisms have been suggested as the anti-cancer mechanisms of surfactin, including apoptosis induction, anti-proliferation of cancer cells, inhibition of angiogenesis, immune response modulation, *etc*. [16,17].

The binding mechanism of surfactin with cancer cells has not been fully understood, but it is believed that the interaction between the lipopeptide and the cell membrane is involved. Studies have suggested that surfactin can bind to the cell membrane of cancer cell through its hydrophobic tail, which can penetrate the membrane and interact with the lipid bilayer [18]. This would disrupt the structure and function of the membrane, thus leading to cell death. The specific receptors of cancer cells for surfactin binding have not been clearly identified or characterized. Additionally, surfactin has been shown to affect the function of membrane proteins and receptors, including those involved in cell signaling pathways and apoptosis [18]. For example, surfactin has been found to modulate the activity of epidermal growth factor receptor (EGFR), which is often overexpressed in cancer cells and involved in tumor growth and survival [19].

In addition, modifications to the structure of surfactin, such as changing the amino acid sequence or modifying the hydrophobic tail, may also lead to ligands with improved binding affinity for cancer cells [20-22]. Hence, further explorations and investigations are needed to identify the specific ligands of cancer cells for surfactin binding and modify the structure of surfactin to improve its anti-cancer properties.

The aim of the current study was to visualize the three-dimensional (3D) structure of surfactin; the processing of surfactin and ligands, coenzyme A ($C_{21}H_{36}N_7O_{16}P_3S$), D-leucine ($C_6H_{13}NO_2$), glycerol ($C_3H_8O_3$), and (R)-3-hydroxytetradecanal ($C_{14}H_{28}O_2$); and the molecular docking of surfactin and ligands to discover the potential binding sites.

2. Methods

2.1. Preparation of surfactin structure

In order to visualize the binding domain and identify the amino acids in the binding pocket, the crystal structure of surfactin (PDB ID: 2VSQ) was imported into chimera from Protein Data Bank (**Figure 1**). As previously reported, an analysis of the amino acid residues in the binding domain of the inhibitor binding site was conducted [23,25]. The ionization and tautomeric states of the amino acid residues were altered in the protein by adding hydrogen atoms. Prior to docking, the water molecules and complexes attached to the receptor molecules were dislodged. Using a virtual screening application, AutoDock Vina, the modified protein was saved in PDBQT format and loaded into PyRx for molecular docking [25,26].

2.2. Generation of ligand dataset

The three-dimensional structures of different target ligand molecules, namely coenzyme A ($C_{21}H_{36}N_7O_{16}P_3S$), D-leucine ($C_6H_{13}NO_2$), glycerol ($C_3H_8O_3$), and (R)-3-hydroxytetradecanal ($C_{14}H_{28}O_2$) were obtained from Protein Data Bank (www.rcsb.org) with the following PDB ID: 1PGP, 1USK, GOL, and 2NPV, respectively [27-29]. Before molecular docking studies were carried out, the protein structure as determined by PDB was modified. The energy of the molecules was reduced, and the water molecules were

eliminated (**Figure 2**).

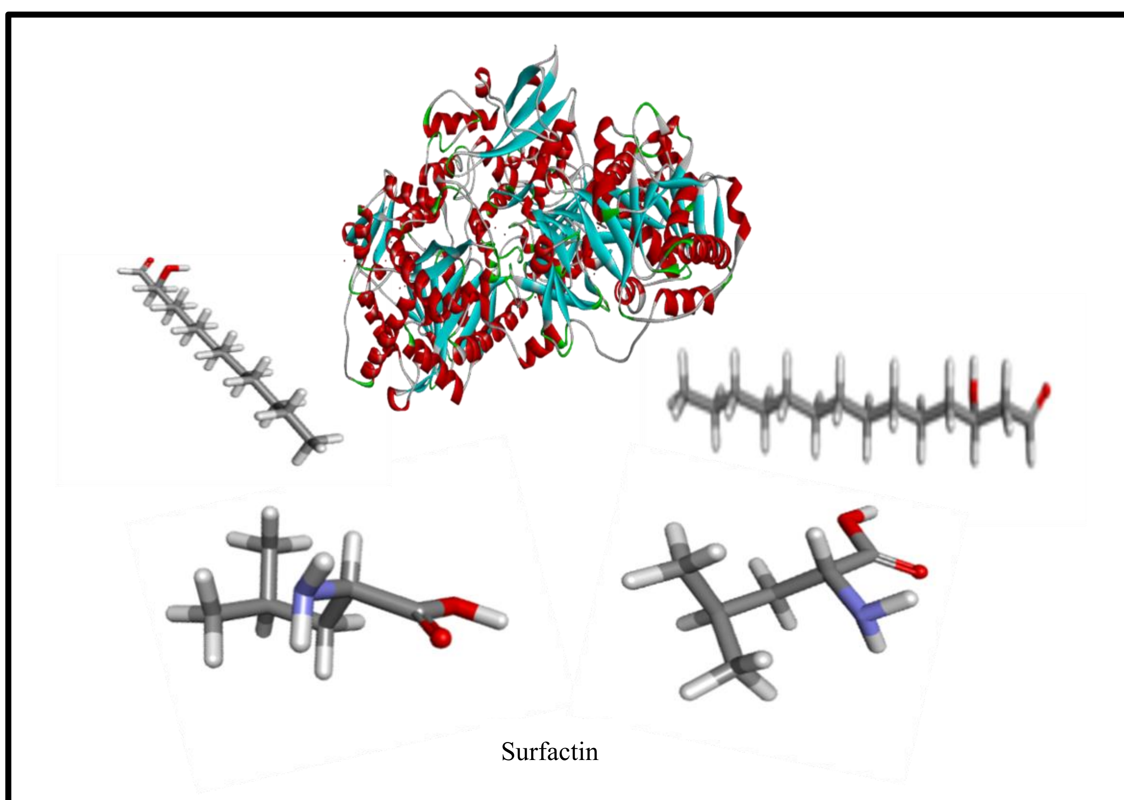

Figure 1. Three-dimensional crystal structure and chemical structure of surfactin

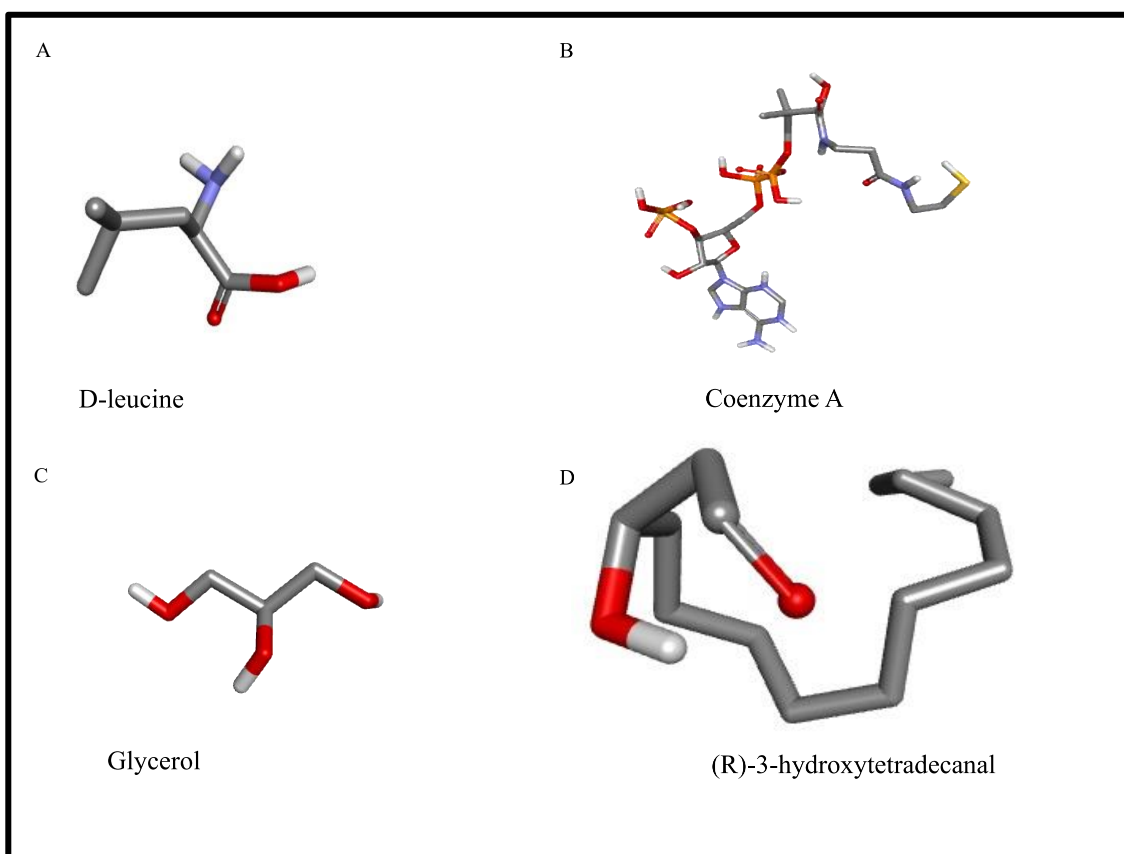

Figure 2. Three-dimensional configuration of ligands before docking

2.3. Docking strategy

The processed PDB files of proteins were loaded into PyRx and converted into macromolecules using the autodock option. Ligand structures were imported using PyRx, and the energy in ligand structures was minimized using an off-force field and conjugate gradient optimization algorithm. Post-energy minimization, ligands were converted into the autodock ligand format. Using Vina Wizard, both the molecule and the ligands were selected, and autodock was initiated. After docking binding affinity for two-dimensional (2D) and 3D binding, the root mean square deviation/upper bound (rmsd/ub) and lower bound (rmsd/lb) were observed. The visualization of receptor-ligand interaction on BIOVIA Discovery Studio and the selection of receptor and ligand were performed. Although docking can ensure binding with available binding sites, knowing the affinity for particular amino acids is desirable.

3. Results and discussions

Drug design is the process of identifying new drugs based on knowledge of their biological targets. Drug design can be categorized into structure-based drug design and ligand-based drug design [30,31]. In structure-based drug design, the 3D structure of the receptor or the target protein is known, whereas in ligand-based drug design, the structure of molecules (ligands) that bind to the target protein of interest is known [32-34]. Interaction between ligands and binding sites is simulated *in silico* drug design and homology modeling. *In silico* drug design employs computer simulation to discover and develop new drugs. However, the complex structures of lipopeptides render this method difficult. When paired with a receptor lipopeptide, particular ligands must be found for physiological reactions to take place [35-37]. Ligands are particles that form complexes with biomolecules to serve biological functions. The orientation of the 3D shape is altered when a ligand binds to a receptor protein, altering the conformation [35-37].

Surfactin has been reported to have anti-proliferative effects on human colon cancer cells, with a significant increase in apoptosis [22]. Six ligands of surfactin have been identified. Among them, D-leucine, the D-alpha-enantiomer of leucine, is a bacterial metabolite. The non-polymer (R)-3-hydroxytetradecanal is covalently linked to polymers or other heterogeneous groups [38]. Around 4% of cellular enzymes use coenzyme A as a substrate. It is known for its function in production and oxidation of fatty acids, as well as the oxidation of pyruvate in the citric acid cycle [39]. Following the identification of surfactin ligands, the molecular docking of these ligands with the lipopeptide was performed for *in silico* drug design with reference to Parween *et al*. and Qasaymeh *et al*. [40,41]. The aim of the current study was to visualize the 3D structure of surfactin; the processing of surfactin and ligands (coenzyme A [$C_{21}H_{36}N_7O_{16}P_3S$], D-leucine [$C_6H_{13}NO_2$], glycerol [$C_3H_8O_3$], and (R)-3-hydroxytetradecanal [C14H28O2]); and the molecular docking of surfactin and ligands to discover potential binding sites.

After docking, nine binding sites with varying affinity were found for D-leucine, coenzyme A, glycerol, and (R)-3-hydroxytetradecanal (**Figure 3**). As shown in **Figure 3**, surfactin binds better with D-leucine and coenzyme A compared to glycerol and (R)-3-hydroxytetradecanal. The binding of surfactin with the selected ligands is illustrated in **Figures 4–5**. In the case of D-leucine, surfactin formed van der Waals bonds (GLY, A: 273, 311; SER, A: 272, 437, 309; VAL, A: 264, 436; GLU, A: 310; ASN, A:792; ILE, A: 312), conventional hydrogen bonds (ARG, A: 268; GLU, A: 793), a carbon-hydrogen bond (SER, A: 267), and an alkyl bond (LEU, A: 308). In the case of coenzyme A, surfactin formed van der Waals bonds (ILE, A: 612, 626, 632; ASN, A: 625, 631; THR, A: 628, 759; SER, A: 814; LYS, A:815), conventional hydrogen bonds (TYR, A: 611; ALA, A: 610), carbon-hydrogen bonds (PRO, A: 609; ASN, A: 631), and covalent bonds (ILE, A: 626; THR, A: 628). In the case of glycerol, surfactin formed only conventional hydrogen bonds (LYS, ARG, THR, TYR), carbon-hydrogen bonds (GLU, PRO), and unfavorable donor-donor bonds (LEU). With (R)-3-hydroxytetradecanal, surfactin formed only unfavorable bonds (ARG, PHE). From these binding analyses, D-leucine and coenzyme A are predicted to be better and stronger ligands for

surfactin.

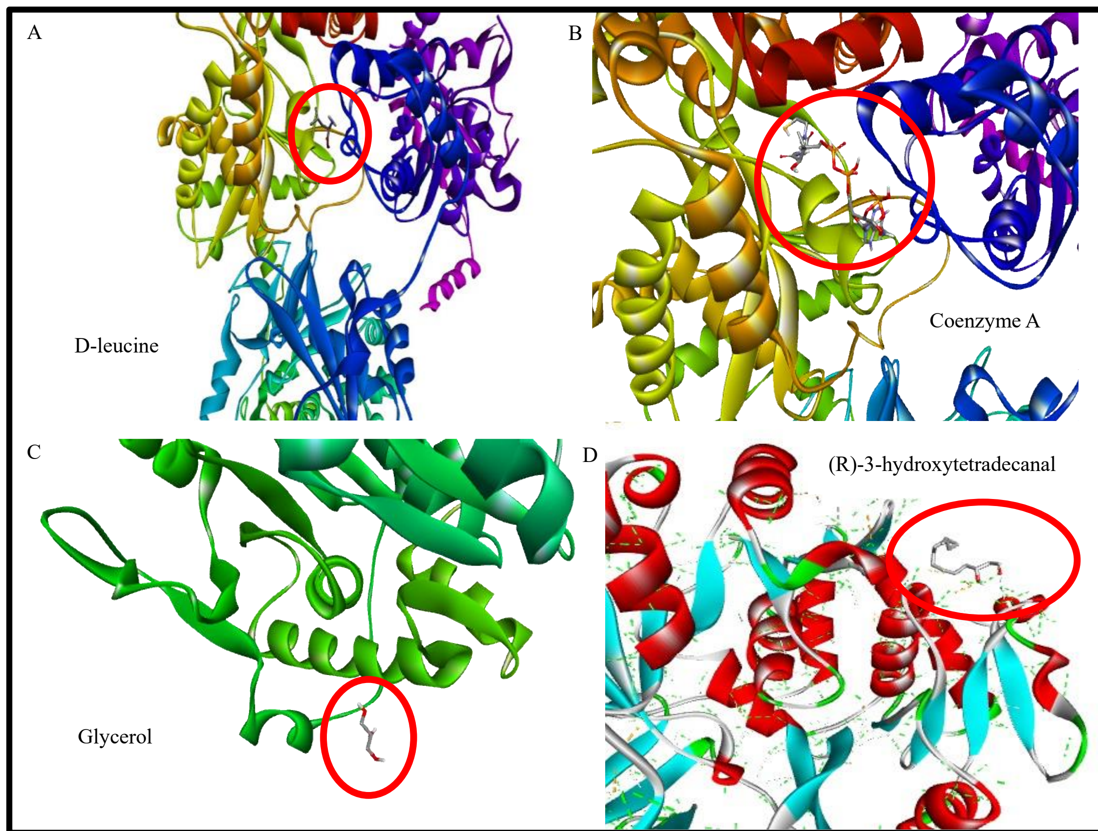

Figure 3. Binding of surfactin with ligands

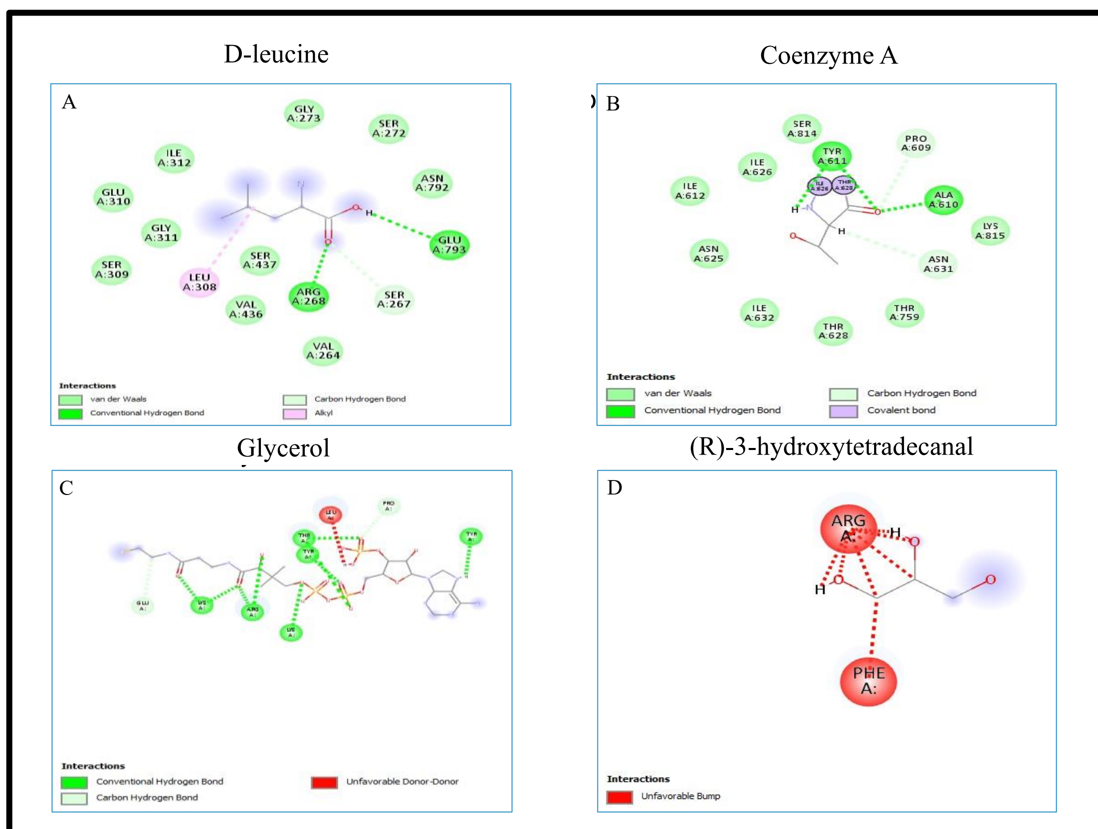

Figure 4. Amino acid binding site of surfactin with ligands

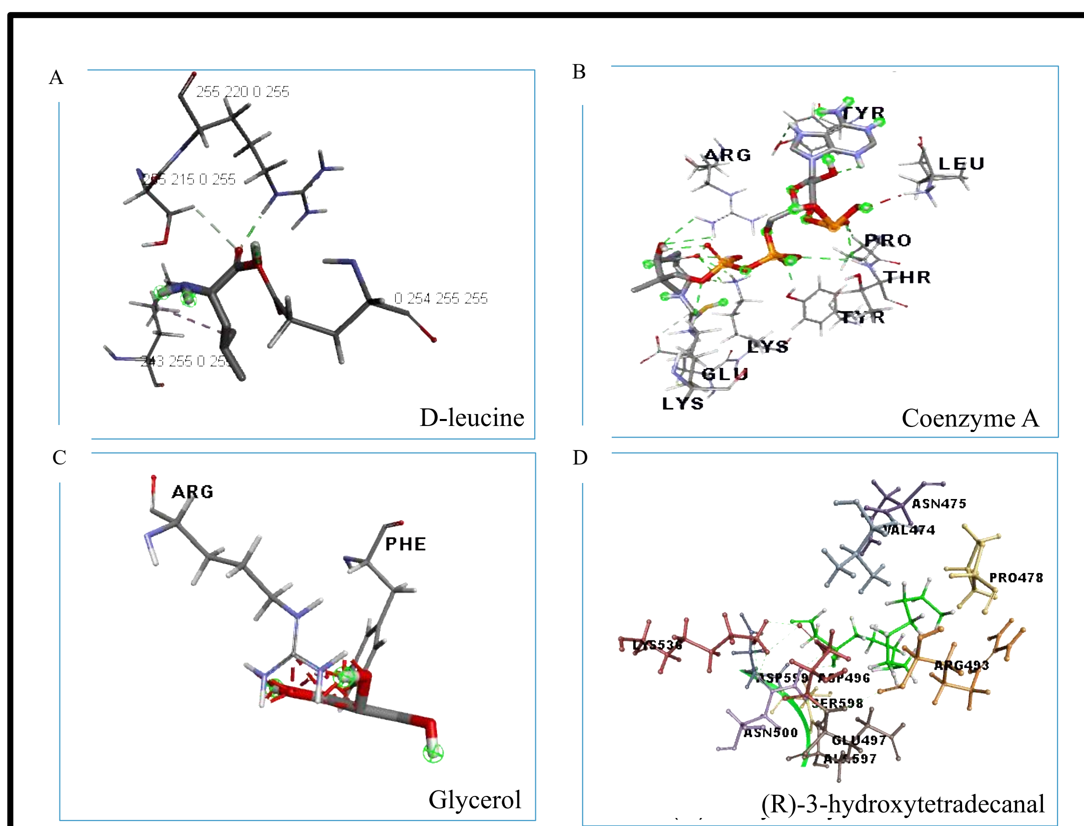

Figure 5. Binding affinity of surfactin with ligands

The docking study revealed that surfactin from *Bacillus* spp. has the highest binding affinity (Ca. -7.5 kcal mol^{-1}) with coenzyme A among the tested ligands but the lowest binding affinity with (R)-3-Hydroxytetradecanal (Ca. -3.5 kcal mol^{-1}). Surfactin was observed to have moderate binding affinity with D-leucine (approximately -4.4 kcal mol^{-1}) and glycerol (approximately -4.1 kcal mol^{-1}). **Table 1** shows the binding affinity of those ligands with surfactin in various conformations, as well as the root mean square deviation (RMSD) of the interacting molecules (protein and ligand).

Table 1. Binding affinity of surfactin with ligands

Ligand	Binding affinity (kcal mol^{-1})	rmsd/ub (root mean square deviation/upper bound)	rmsd/lb (root mean square deviation/lower bound)
D-leucine	-4.6	0	0
	-4.5	2.577	2.216
	-4.4	25.399	24.194
	-4.4	29.603	29.158
	-4.4	64.989	63.672
	-4.3	63.683	62.843
	-4.3	31.076	30.266
	-4.3	28.558	27.722
	-4.3	57.221	56.019

(Continued on next page)

(Continued from previous page)

Ligand	Binding affinity (kcal mol^{-1})	rmsd/ub (root mean square deviation/upper bound)	rmsd/lb (root mean square deviation/lower bound)
Coenzyme A	-7.7	0	0
	-7.6	43.203	40.274
	-7.6	46	42.974
	-7.6	44.764	41.141
	-7.6	11.762	6.135
	-7.5	48.812	45.186
	-7.5	41.543	38.881
	-7.4	10.308	7.804
	-7.4	7.879	5.444
Glycerol	-4.1	0	0
	-4	27.277	26.221
	-4	2.324	0.689
	-4	27.36	26.286
	-3.9	51.725	51.252
	-3.8	20.862	20.14
	-3.8	24.046	23.339
	-3.8	24.179	23.483
	-3.7	2.275	1.486
(R)-3-hydroxytetradecanal	-3.9	0	0
	-3.8	19.391	17.209
	-3.8	3.302	1.626
	-3.5	15.995	13.512
	-3.5	5.453	2.825
	-3.5	16.391	13.991
	-3.4	18.358	16.644
	-3.4	16.969	14.778
	-3.3	16.688	14.711

Due to their high availability as metabolites and low binding affinity, D-leucine, and coenzyme A are highly applicable as binding ligands for surfactin. In order to test the effectiveness of these peptides, *in vivo* studies on animal models can be carried out following the completion of drug design.

4. Conclusions

We conducted a computational study to assess the binding potential of surfactin from *Bacillus* spp. to identify new potential candidates for the treatment of cancer. Thus, according to our *in silico* study, surfactin may act as a potential drug that can be used as a promising anti-cancer agent. Nevertheless, further experimental studies are needed to investigate the ligand binding and anti-cancer potentials of such surfactin-like molecules. While these studies are promising, more research is needed to fully understand the potential of surfactin as an anticancer agent. Additionally, the use of surfactin in cancer treatment would require further testing and evaluation to determine its safety and efficacy in humans.

Disclosure statement

The authors declare no conflict of interest.

Author contributions

M.A.A., U.T.F., M.F., S.D., and M.A.S. were involved in research conceptualization and design; M.A.A. and U.T.F. took part in the collection and/or assembly of data; U.T.F., M.F., S.D., and M.A.S. were involved in data analysis and interpretation; M.F. and M.A.S. took part in manuscript writing; and M.F., S.D., and M.A.S. were involved in the critical revision of the manuscript. All authors read and approved the final manuscript.

References

[1] Dan AK, Manna A, Ghosh S, et al., 2021, Molecular Mechanisms of the Lipopeptides from *Bacillus subtilis* in the Apoptosis of Cancer Cells – A Review on its Current Status in Different Cancer Cell Lines. Adv Cancer Biol – Metastasis, 3: 100019. https://linkinghub.elsevier.com/retrieve/pii/S2667394021000198

[2] Harimurti S, Widada H, Arsito PN, et al., 2022, Molecular Docking for Evaluation of Piperine Affinity to the Colon Cancer Receptor. KnE Med, 2022: 472–479. https://knepublishing.com/index.php/KnE-Medicine/article/view/11900

[3] Vaishnav N, Khare N, Katariya PK, et al., 2020, To Study the Effect of Harmine Against DNMT1 for the Treatment of Cervical Cancer Through Molecular Docking Studies. International Journal of Pharmacy and Biological Science, 10(3): 125–132.

[4] Falzone L, Salomone S, Libra M, 2018, Evolution of Cancer Pharmacological Treatments at the Turn of the Third Millennium. Front Pharmacol, 9: 1–26. https://www.frontiersin.org/article/10.3389/fphar.2018.01300/full

[5] Pham TH, Nguyen HN, Le TTH, 2018, In Silico Screening, Design and Synthesis of Novel Inhibitors against Histone Deacetylase (HDAC). VNU J Sci Med Pharm Sci, 34(1): 20. https://js.vnu.edu.vn/MPS/article/view/4100

[6] Kaur B, Rolta R, Salaria D, et al., 2022, An In Silico Investigation to Explore Anti-Cancer Potential of *Foeniculum vulgare* Mill. Phytoconstituents for the Management of Human Breast Cancer. Molecules, 27(13): 4077. https://www.mdpi.com/1420-3049/27/13/4077

[7] Khalid I, Jafar TH, Unar A, et al., 2021, In-Silico Identification of Anticancer Compounds; Ligand-Based Pharmacophore Approach Against EGFR Involved in Breast Cancer. Adv Breast Cancer Res, 10(03): 120–132. https://www.scirp.org/journal/doi.aspx?doi=10.4236/abcr.2021.103010

[8] Ferdous UT, Shishir MA, Khan SN, et al., 2018, *Bacillus* spp.: Attractive Sources of Anti-Cancer and Anti-Proliferative Biomolecules. Microb Bioact, 1(1): E033–E045. https://doi.org/10.25163/microbbioacts.11005B0408130818

[9] Jujjavarapu SE, Dhagat S, 2018, In Silico Discovery of Novel Ligands for Antimicrobial Lipopeptides for Computer-Aided Drug Design. Probiotics Antimicrob Proteins, 10(2): 129–141. http://link.springer.com/10.1007/s12602-017-9356-9

[10] Jujjavarapu SE, Dhagat S, Kurrey V, 2018, Identification of Novel Ligands for Therapeutic Lipopeptides: Daptomycin, Surfactin and Polymyxin. Curr Drug Targets, 19(13): 1589–1598. http://www.eurekaselect.com/157849/article

[11] Wu Y-SS, Ngai S-CC, Goh B-HH, et al., 2017, Anticancer Activities of Surfactin and Potential Application of Nanotechnology Assisted Surfactin Delivery. Front Pharmacol, 8: 761. http://www.ncbi.nlm.nih.gov/pub med/29123482

[12] Vo TTT, Wee Y, Cheng H, Wu C, et al., 2023, Surfactin Induces Autophagy, Apoptosis, and Cell Cycle Arrest in Human Oral Squamous Cell Carcinoma. Oral Dis, 29(2): 528–541. https://onlinelibrary.wiley.com/doi/10.1111/odi.13950

[13] Fayed MAA, El-Behairy MF, Abdallah IA, et al., 2021, Structure- and Ligand-Based In Silico Studies towards the Repurposing of Marine Bioactive Compounds to Target SARS-CoV-2. Arab J Chem, 14(4): 103092. https://linkinghub.elsevier.com/retrieve/pii/S1878535221001076

[14] Braz HLB, Silveira JA de M, Marinho AD, et al., 2020, In Silico Study of Azithromycin, Chloroquine and Hydroxychloroquine and Their Potential Mechanisms of Action Against SARS-CoV-2 infection. Int J Antimicrob Agents, 56(3): 106119. https://linkinghub.elsevier.com/retrieve/pii/S0924857920303022

[15] Ahsan Z, Khare N, Jha AK, et al., 2020, The Discovery of Potential Dnmt1 Inhibitors: A Combination of Virtual Screening and Molecular Docking Studies. Int J Res Trends Innov, 5(10): 17–22.

[16] Vo TTT, Lee C-W, Wu C-Z, et al., 2020, Surfactin from *Bacillus subtilis* Attenuates Ambient Air Particulate Matter-Promoted Human Oral Cancer Cells Metastatic Potential. J Cancer, 11(20): 6038–6049. https://www.jcancer.org/v11p6038.htm

[17] Niode NJ, Adji A, Rimbing J, et al., 2021, In Silico and In Vitro Evaluation of the Antimicrobial Potential of *Bacillus cereus* Isolated from Apis dorsata Gut Against *Neisseria gonorrhoeae*. Antibiotics, 10(11): 1401. https://www.mdpi.com/2079-6382/10/11/1401

[18] Sen R, 2010, Surfactin: Biosynthesis, Genetics and Potential Applications, in Biosurfactants Advances in Experimental Medicine and Biology, Springer, New York, 316–323.

[19] Hasegawa Y, Takahashi M, Ariki S, et al., 2017, Surfactant Protein A Down-Regulates Epidermal Growth Factor Receptor by Mechanisms Different from Those of Surfactant Protein D. J Biol Chem, 292(45): 18565–18576.

[20] Bonmatin J-M, Laprevote O, Peypoux F, 2012, Diversity Among Microbial Cyclic Lipopeptides: Iturins and Surfactins. Activity-Structure Relationships to Design New Bioactive Agents. Comb Chem High Throughput Screen, 6(6): 541–556.

[21] Liu X, Tao X, Zou A, et al., 2010, Effect of the Microbial Lipopeptide on Tumor Cell Lines: Apoptosis Induced by Disturbing the Fatty Acid Composition of Cell Membrane. Protein Cell, 1(6): 584–594.

[22] Tank JG, Pandya RV, 2022, Anti-Proliferative Activity of Surfactins on Human Cancer Cells and Their Potential Use in Therapeutics. Peptides, 155: 170836. https://linkinghub.elsevier.com/retrieve/pii/S0196978122001024

[23] Sur VP, Sen MK, Komrskova K, 2021, In Silico Identification and Validation of Organic Triazole Based Ligands as Potential Inhibitory Drug Compounds of SARS-CoV-2 Main Protease. Molecules, 26(20): 6199. https://www.mdpi.com/1420-3049/26/20/6199

[24] Uddin KM, Hosen MA, Khan MF, et al., 2022, Investigation of Structural, Physicochemical, Pharmacokinetics, PASS Prediction, and Molecular Docking Analysis of SARS-Cov-2 Against Methyl 6-O-Myristoyl-α-D-Glucopyranoside Derivatives. Philipp J Sci, 151: 2215–2231.

[25] Afriza D, Suriyah WH, Ichwan SJA, 2018, In Silico Analysis of Molecular Interactions Between the Anti-Apoptotic Protein Survivin and Dentatin, Nordentatin, and Quercetin. J Phys Conf Ser, 1073: 032001. https://iopscience.iop.org/article/10.1088/1742-6596/1073/3/032001

[26] Bhowmik A, Biswas S, Hajra S, et al., 2021, In Silico Validation of Potent Phytochemical Orientin as Inhibitor of SARS-Cov-2 Spike and Host Cell Receptor GRP78 Binding. Heliyon, 7(1): e05923. https://linkinghub.elsevier.com/retrieve/pii/S2405844021000281

[27] Poupon A, Janin J, 2010, Analysis and Prediction of Protein Quaternary Structure. Methods Mol Biol, 609: 349–364. http://www.ncbi.nlm.nih.gov/pubmed/20221929

[28] Biasini M, Bienert S, Waterhouse A, et al., 2014, SWISS-MODEL: Modelling Protein Tertiary and Quaternary Structure Using Evolutionary Information. Nucleic Acids Res, 42: W252–W258. http://www.ncbi.nlm.nih.gov/pubmed/24782522

[29] Nahar M, Shishir A, Karim MM, et al., 2014, Cloning, Expression and Structure Simulation of Keratinase from *Bacillus licheniformis* Strain MZK05. Malaysian Journal of Microbiology, 12(2): 182–190.

[30] Odoemelam CS, Hunter E, Simms J, et al., 2022, In Silico Ligand Docking Approaches to Characterise the Binding of Known Allosteric Modulators to the Glucagon-Like Peptide 1 Receptor and Prediction of ADME/Tox Properties. Appl Biosci, 1(2): 143–162. https://www.mdpi.com/2813-0464/1/2/10

[31] Rajak P, Roy S, Pal AK, et al., 2021, In Silico Study Reveals Binding Potential of Rotenone at Multiple Sites of Pulmonary Surfactant Proteins: A Matter of Concern. Curr Res Toxicol, 2: 411–423. https://linkinghub.elsevier.com/retrieve/pii/S2666027X21000414

[32] Koperuncholan M, Baskaran T, Aravindha V, 2022, In Silico Analysis and Molecular Docking Studies of Anti-HIV Ligand Baurenol Against Mutant Hiv-1 Reverse Transcriptase. Bull Environ Pharmacol Life Sci, 11(4): 76–84.

[33] Yu W, MacKerell AD, 2017, Computer-Aided Drug Design Methods, in Antibiotics: Methods in Molecular Biology, Humana Press, New York, 85–106. https://doi.org/10.1007/978-1-4939-6634-9_5

[34] Roche DB, McGuffin LJ, 2016, In Silico Identification and Characterization of Protein-Ligand Binding Sites, in Computational Design of Ligand Binding Proteins Methods in Molecular Biology, Humana Press, New York, 1–21. http://link.springer.com/10.1007/978-1-4939-3569-7_1

[35] Khusro A, Aarti C, Agastian P, 2019, In Silico Modelling and Molecular Docking Insight of Bacterial Peptide for Anti-Tubercular and Anticancer Drug Designing. Trends Bioinforma, 13(1): 1–9. http://www.scialert.net/abstract/?doi=tb.2020.1.9

[36] Li H, Leung K-S, Wong M-H, et al., 2016, Correcting the Impact of Docking Pose Generation Error on Binding Affinity Prediction. BMC Bioinformatics, 17(S11): 308. http://bmcbioinformatics.biomed central.om/articles/10.1186/s12859-016-1169-4

[37] Vauquelin G, Packeu A, 2009, Ligands, Their Receptors and … Plasma Membranes. Mol Cell Endocrinol, 311(1–2): 1–10. https://linkinghub.elsevier.com/retrieve/pii/S0303720709003955

[38] Nnyigide OS, Lee S-G, Hyun K, 2019, In Silico Characterization of the Binding Modes of Surfactants with Bovine Serum Albumin. Sci Rep, 9(1): 10643. https://www.nature.com/articles/s41598-019-47135-2

[39] Pal A, Curtin JF, Kinsella GK, 2021, In Silico and In Vitro Screening for Potential Anticancer Candidates Targeting GPR120. Bioorg Med Chem Lett, 31: 127672. https://linkinghub.elsev ier.com/retrieve/pii/S0960894X20307836

[40] Qasaymeh RM, Rotondo D, Oosthuizen CB, et al., 2019, Predictive Binding Affinity of Plant-Derived Natural Products Towards the Protein Kinase G Enzyme of *Mycobacterium tuberculosis* (*Mt*PknG). Plants, 8(11): 477. https://www.mdpi.com/2223-7747/8/11/477

[41] Parween A, 2020, Molecular Docking of Quinolone against INHA to Treat Tuberculosis. Int J Res Appl Sci Eng Technol, 8(6): 2421–2427. http://ijraset.com/fileserve.php?FID=29915

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.