Vol:2, Pg: 32-37, Yr: 2021-AJABTR

Antibiofilm Activity of Phytocompounds against Biofilm forming Proteins of *Staphylococcus aureus* and *Pseudomonas aeruginosa* - *In silico* study

Gidugu Bhargavi Lakshmi[1], Sayan Bardhan[1], Kunal Vora[1*], Arpita Ghosh[1]

[1]SHRM Biotechnologies Pvt Ltd, Kolkata, West Bengal, India

*Corresponding: kunal.vora@shrmbio.com

Abstract

Biofilms are the syntrophic consortia of sessile microcolonies that remain adhered to biotic and abiotic surface with the help of self-secreted extracellular polymeric substances (EPS). The biofilms, formed by both Gram-positive and Gram-negative bacteria, help them to survive extreme conditions such as exposure to heat shock, antibiotics and lack of nutrients. Therefore, this can lead to severe chronic infection on wounds, diabetic ulcers and medical implants. In this paper, *in-silico* studies were performed on biofilm forming proteins to study the role of various phytocompounds in eradication of biofilm formation by some of Abiotic surfaces can attract bacteria due to the presence of nutrients on them, whereas biotic surfaces such as human and plant tissue can themselves be a source of nutrients for microorganisms [1, 2]. the most popular Gram positive strains (*Staphylococcus aureus*) and Gram-negative strain (*Pseudomonas aeruginosa*). The selected ligands were thoroughly observed for its molecular electrostatic property and molecular docking was done to predict the 2D protein-ligand interactions. It was observed that nimbin showed maximum interaction with the biofilm forming proteins of both Gram-positive and Gram-negative bacteria.

Keywords: Biofilm, *S. aureus*, *P. aeruginosa*, anitibiofilm, phytrocompounds, molecular interaction

1. Introduction

Therefore, microorganisms irreversibly attach to the nutrient rich surface and grow producing a syntrophic consortium. These aggregations of bacterial communities are known as biofilms [3, 4]. They are mainly

found in submerged areas with or without any contact to water. The biofilm consists of unique bacterial architecture which is important for their survival and interaction. Formation of biofilms is advantageous to bacteria because it provides drug resistance, help them tolerate unfavourable conditions. Moreover, the slimy extracellular polysaccharide substance (EPS) matrix appearing like a sticky substance that covers the bacterial community provides protection against phagocytosis [5, 6].

Initially, the free-floating bacteria that remain as suspended, known as planktonic bacteria, do not have the adherence property required for the formation of biofilm. However, when they transform into the sessile form, these microbial cells gain that character which helps in attachment to the preferred surface [7 - 9]. Reversible attachment of planktonic cells involves the initial attachment of these cells to the surface via weak Vander Waal's forces. It only takes upto few seconds and hence reversible. These initial interactions are hydrophobic and non-specific in nature [9]. The irreversible attachment of the cells occurs when the planktonic cells start to differentiate into sessile cells by changing their gene expression pattern. The adhesion of the cells to the surface is facilitated by extracellular polymeric substance (EPS) and this attachment takes few minutes to occur. In biofilms the bacterial cells communicate with each other by quorum sensing, which means that the cell population density is controlled by various gene regulation steps [8]. When the bacterial population keeps on increasing, certain auto inducers start accumulating in the environment which in turn helps the bacterial cells to alter their regulating genes for certain beneficial life processes as the cells are clumped together [7].

In this work, we will be focusing on the antibiofilm activity of major phytocompounds against the biofilm forming proteins of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

2. Materials and methods

Docking. Molecular docking is one of the most used methods to predict the structure of various drugs which are being designed and also to understand the binding interactions between the molecules. The interaction of a ligand with its target site is observed through docking. Docking has been done between the antibiofilm formimg protein against the biofilm forming protein individually using AutoDock Vina (9). The interaction between the proteins has been checked

3. Results and Discussion

The molecular docking interactions showed that nimbin showed maximum inhibition of the biofilm forming protein of *S. aureus* and *P. aeruginosa* in comparison to other phytocompounds that interacted with the protein. It was further observed that phytocompounds showed efficacy in the inhibition of the biofilm forming proteins of the two major organisms *S. aureus* and *P. aeruginosa* (Table 1, Figure 1).

Table 1: Binding energy of the molecular docking interaction between the biofilm forming protein and phytocompounds

Organism	**Biofilm forming protein**	**Phytocompound**	**Binding Energy (Kcal/mole)**
Staphylococcus aureus	3TIP	Curcumin	-6.00
		Eugenol	-4.09
		Quercetin	-5.75
		Nimbin	-6.26
		Gingerol	-5.62
Pseudomonas aeruginosa	3ZYB	Curcumin	-7.17
		Eugenol	-5.50
		Quercetin	-6.74
		Nimbin	-7.42
		Gingerol	-6.49

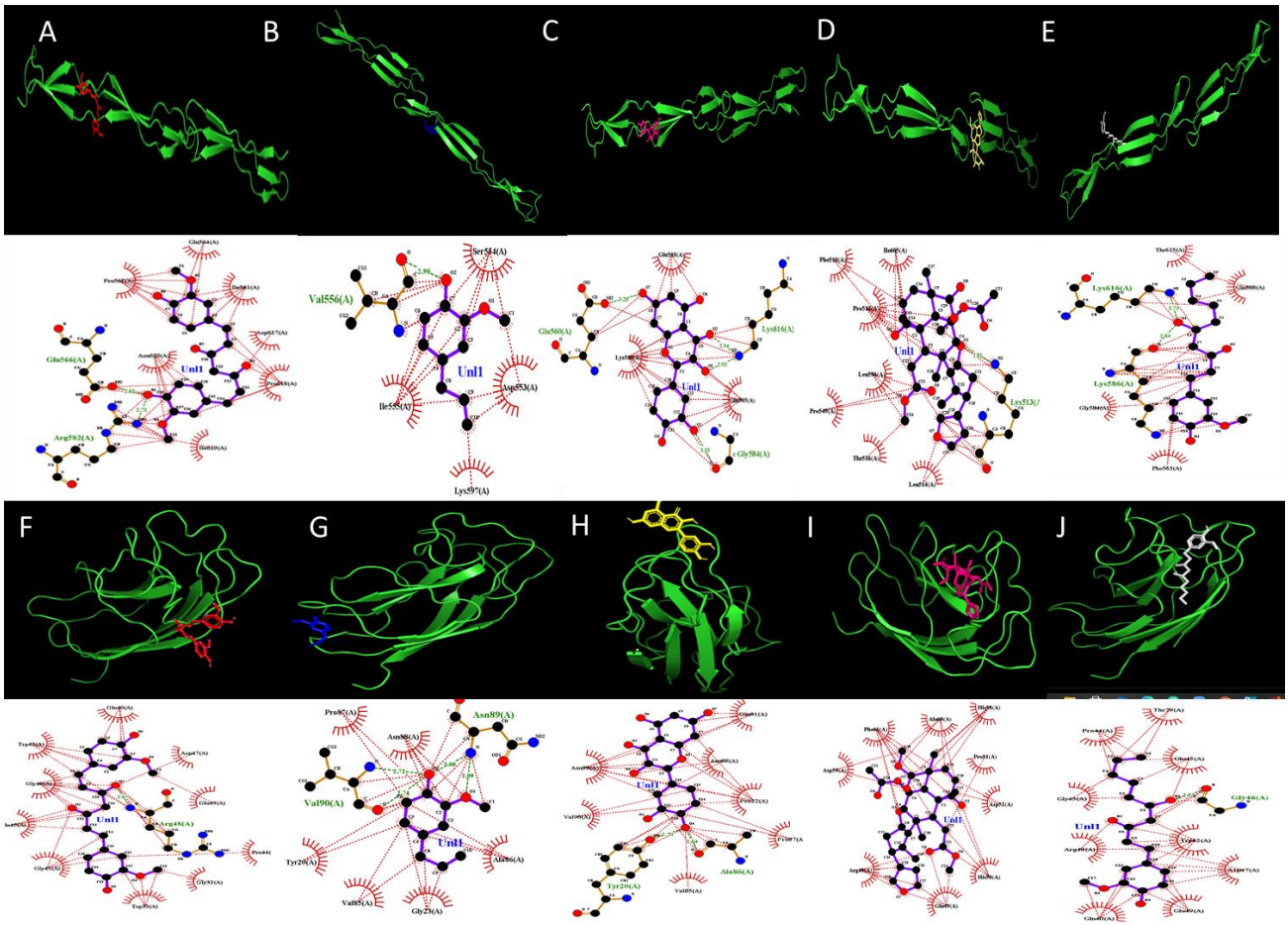

Figure 1: Molecular docking interaction of the biofilm forming proteins of *S. aureus* and *P. aeruginosa* with the phytocompounds.

4. Conclusion

The study showed nimbin showed maximum interaction with the biofilm forming proteins of *S. aureus* and *P. aeruginosa*. This depicts that phytocompounds can be used as alternate therapeutics in the inhibition of the bifilm formed by major organisms.

References

1. Lahiri, D., Dash, S., Dutta, R. *et al.* Elucidating the effect of anti-biofilm activity of bioactive compounds extracted from plants. *J Biosci* **44,** 52 , 2019
2. Pooi Y. Chung, Yien S. Toh, Anti-biofilm agents: recent breakthrough against multi-drug

resistant *Staphylococcus aureus*, *Pathogens and Disease*, Volume 70, Issue 3, Pages 231–239,2014.

3. Lahiri, D., Nag, M., Dutta, B. et al. Catechin as the Most Efficient Bioactive Compound from Azadirachta indica with Antibiofilm and Anti-quorum Sensing Activities Against Dental Biofilm: an In Vitro and In Silico Study. Appl Biochem Biotechnol **193,** 1617–1630, 2021.
4. Lahiri D., Nag M., Dutta B., Dash S., Ghosh S., Ray R. Synergistic Effect of Quercetin with Allicin from the Ethanolic Extract of Allium cepa as a Potent AntiQuorum Sensing and Anti-Biofilm Agent Against Oral Biofilm. In: Ramkrishna D., Sengupta S., Dey Bandyopadhyay S., Ghosh A. (eds) Advances in Bioprocess Engineering and Technology. Lecture Notes in Bioengineering. Springer, Singapore. 2021.
5. Lahiri, D., Nag, M., Dutta, B., Dey, S., Mukherjee, D., Joshi, S. J., & Ray, R. R.. Anti biofilm and anti-quorum sensing activities of eugenol and linalool from Ocimum tenuiflorum against Pseudomonas aeruginosa biofilm. Journal of Applied Microbiology 2021
6. Dutta B., Nag M., LahiriD., Ray R.R. Analysis of Biofilm Matrix by Multiplex Fluorescence In Situ Hybridization and Confocal Laser Scanning Microscopy During Nosocomial Infections. Analytical Methodologies for Biofilm Research. Springer Protocols Handbooks. Springer, New York, NY. https:/doi.org/10.1007/978-1-0716-1378-8_8, 2021
7. Soltani, Emad; Farrokhi, Effat; Zamanzad, Behnam; Shahini Shams Abadi, Milad; Deris, Fatemeh; Soltani, Amin; Gholipour, Abolfazl . Prevalence and distribution of adhesins and the expression of fibronectin-binding protein (FnbA and FnbB) among Staphylococcus aureus isolates from Shahrekord Hospitals. BMC Research Notes, 12(1), 49, 2019.
8. Rutherford, S. T.; Bassler, B. L. . Bacterial Quorum Sensing: Its Role in Virulence and Possibilities for Its Control. Cold Spring Harbor Perspectives in Medicine, 2(11), a012427–a012427.2012

9. Jørgensen, Nis; Zobek, Natalia; Dreier, Cindy; Haaber, Jakob; Ingmer, Hanne; Larsen, Ole; Meyer, Rikke (2016). Streptokinase Treatment Reverses Biofilm-Associated Antibiotic Resistance in Staphylococcus aureus. Microorganisms, 4(3), 36, 2016