International Journal for Research in Applied Sciences and Biotechnology

ISSN: 2349-8889
Volume-7, Issue-6 (November 2020)

www.ijrasb.com

https://doi.org/10.31033/ijrasb.7.6.17

Review Article: The Role of Bacterial Biofilms in Chronic Diseases

Wedad Salih Dawood
College of Veterinary/Microbiology, University of Diyala, IRAQ

Corresponding Author: wedad.s@uodiyala.edu.iq

ABSTRACT

Diseases usually take place in individuals due to infection that can be occurs more than one time, and also can reach up to years, and the bacterial and microbial biofilms play main roles on more than 75% of the whole infections, these roles are responsible for many points such as creating chronic diseases, resistance the drug, effect the immune system, contaminating the medical equipments and devices, and clinical infections. The microbial biofilms can be single or accumulated in colonies and layers in the host, and cause the chronic diseases through weakening the immune system and even attack the antibiotic treatments that given to the patient and make it without advantage and cannot help in recovery. In this review, it was focused on how bacterial biofilms play an important role in foot ulcer in diabetic patients, and it was concluded that infections with microbial biofilms may leads to decrease the immune system and leads to chronic diseases.

Keywords- Bacterial biofilms, immune system, chronic diseases, diabetes.

I. INTRODUCTION

Throughout the infection that caused by bacterial biofilm in particular, as well as the microbial infection in general, the host is represented by the organism, while the immune system of the host (organism) considered as the antibacterial and an antimicrobial as if a treatment, but for chronic diseases, this infection can takes more time, and can reach up to years [(1-4)]. The bacterial biofilms play important roles on more than 75% of the whole infections, these roles focused on the following points [(5-6)]:

1. It can be the cause of creating the chronic infections.
2. Drug fighting.
3. Response of the immune system
4. Pollution and contamination to the medical equipments and devices.
5. More than 80% of clinical infections caused by biofilms.

Bacterial biofilms may also improve and enhance the microorganisms against unfavorable conditions of the environment. Microbiota can exist either in multiple or in single; it is also expressed as polymicrobial or monomicrobial respectively, the genomic analysis assumed that most bacterial biofilms presence in human body in a polymicrobial form [(7-9)].

Figure 1 show the polymicrobial biofilms in dental plaque, while figure 2 show the monomicrobial biofilm which usually represented by anaerobic bacteria which do not require oxygen.

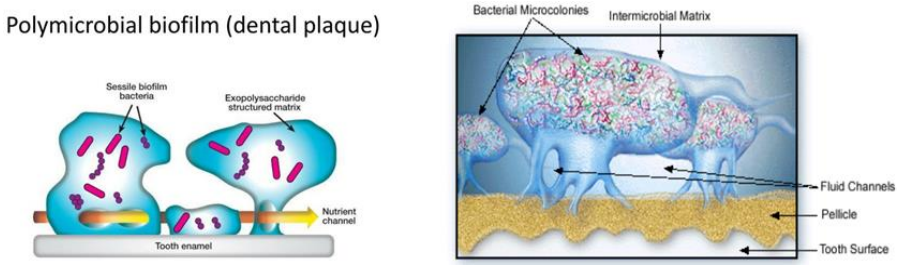

Figure 1: Dental plaque shows the microbial biofilm [(10)]

Figure 2: Monobacterial represented by anaerobic bacteria [(11)]

ISSN: 2349-8889
Volume-7, Issue-6 (November 2020)

www.ijrasb.com https://doi.org/10.31033/ijrasb.7.6.17

Important differences between mono and poly bacterial infection, for instance, the infection of conjunctivitis that caused by *S. pneumonia*, this can be noticed in the frequency and the dominant of the infection.

II. BACTERIAL BIOFILMS CAN CAUSE AND CREATE CHRONIC INFECTION

Throughout a severe infection, the host is presented by the organism for quite small time, and it was disinfected through the immune system using antimicrobial treatment drugs or without it. In chronic infection the process is quite different because it takes more time (moths or sometimes years), therefore the body that have chronic infection, can be a host that provide an ideal environment that play an important role which extend the interaction between host and infective microbes creations, this will eventually leads to create synergistic or mutualistic interactions that resulted in the formation of bacterial biofilms as well as the possibility of transferring in genes. For example, bacterial biofilm responsible for chronic wounds in diabetic patients, the chronic wound beds inhabitants (gram-negative and gram-positive bacteria) which often create a mixture of microbial biofilms that cause many infections [12, 13].

III. DRUG FIGHTING (RESISTANCE)

One of the most important individuality of the bacterial biofilms is its resistance to the drugs, precisely antibiotics, the cells of the microbes that allied to the biofilms developed and grown more than 1000 times in its resistance toward the therapy and the treatment of the antibiotic drugs than other cells (planktonic cells), it is expected that the matrix of extracellular of the bacterial biofilm is accountable and in charge for the resistance and tolerance toward treatment of the antimicrobial drug through its behaves as a physical blockade against the antibiotic [14, 15].

Latest studies indicate that the mechanism of the resistance against antimicrobial drugs established the presence of both bacterial biofilms and the planktonic cells as well. The genetic contents can be transferred via the involvement of HGT (Horizontal gene transfer), this transfer can be occurred in conjugation, transformation as well as transduction [16, 17].

The DNA of bacteria form a certain cells called (lysed cells) that grow its capable cells from the same species, and this occurs via inter / or intra transformation of the species and the process that take place at this time called recombination of genes. The antimicrobial resistance to the drugs will be kept due to natural selection; this can be shown in the existence of the biofilm which is almost 1.6 x10^4 greater than planktonic cells, this can explain the volume of the bacterial biofilm and its resistance to the antimicrobial drugs (antibiotic resistance) [18, 19].

Figure 3 shows the mechanism of drug resistance, while figure 4 represent a scheme that shows the difference between resistance bacteria, and non-resistance bacteria against antibiotics.

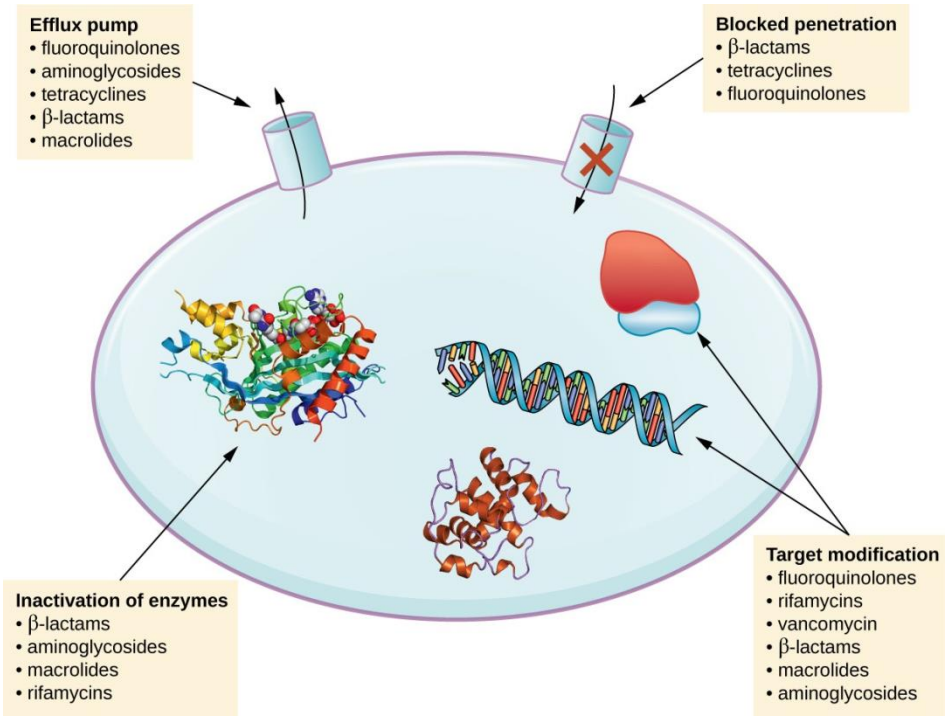

Figure 3: the mechanism of cell development in its resistance against antimicrobial drugs [20]

ISSN: 2349-8889
Volume-7, Issue-6 (November 2020)

https://doi.org/10.31033/ijrasb.7.6.17

Figure 4 represent a scheme that shows the simple differences between the 2 types of bacteria, precisely the resistance bacteria and the non-resistance bacteria.

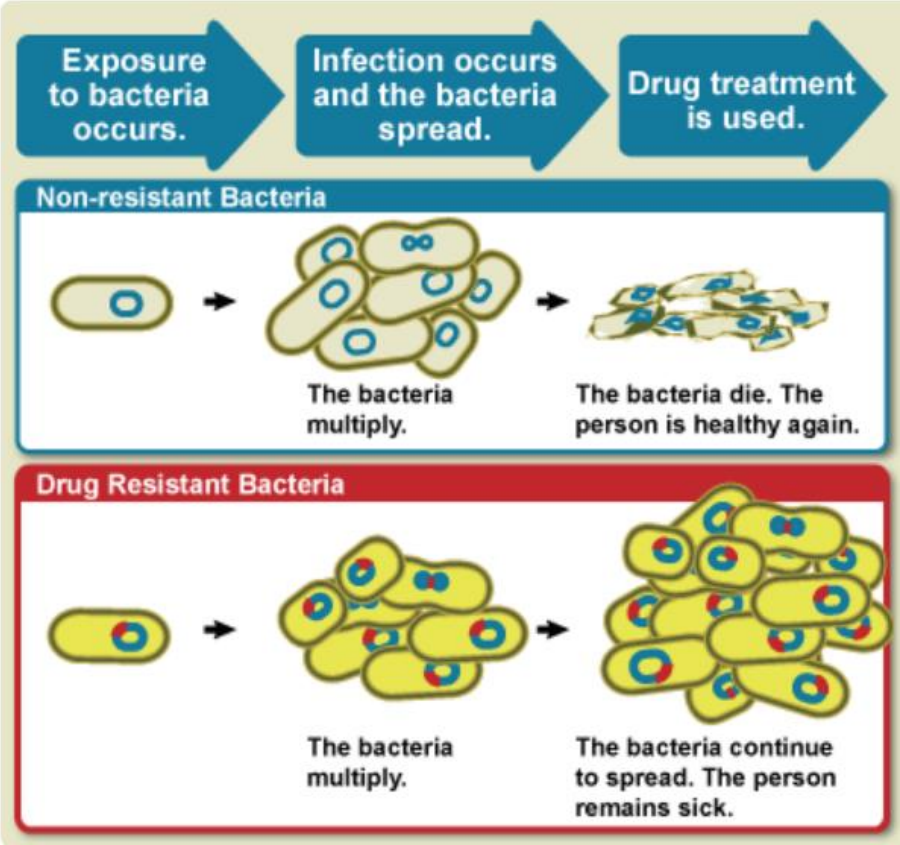

Figure 4: simple scheme shows the difference between resistance / and non-resistance bacteria [21]

IV. RESPONSE OF THE IMMUNE SYSTEM

The famous name of the bacterial biofilms changed the response of the immune system in the direction to attack the pathogens. The response toward inflammation rise and increased via the directions of the host in opposition to the micro organs that cause infections in order to protect the cells of the host and kill the attacker pathogens. On the contrary there are many situations that involve clinical chronic infection by which the response of the immune system toward pathogens has additional harms rather than helps to the cells, mostly the existence of the bacterial biofilms can be the main reason of uncertain attack [22-24].

V. MEDICAL DEVISES AND EQUIPMENTS CONTAMINATION

It is well know the contamination that caused by the bacterial and microbial biofilms to the medical apparatuses and devises and as much as it is used as much as the possibility of infection is increased due to the virulence role of the microbial biofilms which eventually cause clinical troubles and difficulties, and honestly, most clinicians and the technicians who works in clinics do not imagine or even think the volume of its consequences, because they based their resolutions on planktonic susceptibilities in vitro and not the susceptibilities of the biofilms itself [25, 26].

Although there is an increasing of the researches in the field of bacterial and microbial biofilms, still there are a lot of difficulties in characterizing them, precisely when implanting the medical apparatuses and devices, and because of this, it is recommended, from the current review point of view, it is suggested to the future studies to focus on evaluation the association and the interaction and the connection between the failure in treatment and the biofilm itself and how to develop a certain compounds that works as an anti biofilm and enhance them [27, 28].

Figure 5 shows the medical device infection [29].

A B

Figure 5: A- Medical devices infections; B- Clumps of St. Epidermidis bacteria, the main infection causes in clinics and hospitals which eventually cause sepsis **(in green color) that accompanied to in the extracellular matrix [29]**

As noticed from figure 5, it is clear the complexation of the bacterial biofilm due to its existence in multi layers as well as its accumulation in communities which enable them to form a surface on the object (medical device) [30].

VI. THE SIGNIFICANCE OF BACTERIAL BIOFILMS IN THE ULCERS FOOT IN DIABETICS

Pouget et al. 2020 mentioned that the main complication in diabetes patients that increase their disability in their daily life and prevent them from doing their ordinary functions is the infection in their feet, which increases the death possibility (mortality) due to amputation in the lower limbs, and also decreases the life style which eventually play an important role in the resistance on the effect of antibiotics and leads to difficulties in the healings of the wound in diabetes patients [31].

The main issue in food ulcers in diabetic patients (DFU) is the distinguishing between colonization and infections that caused by bacterial biofilms due to the interaction between biofilms and the bacteria, as a result of this, various species of bacteria could be considered as non-pathogenic (unable to sustain a chronic disease), but in fact it is not and cause clinical complications due to the presence of microorganism [32].

The formation of different bacterial biofilms is shown in figure 6 [33].

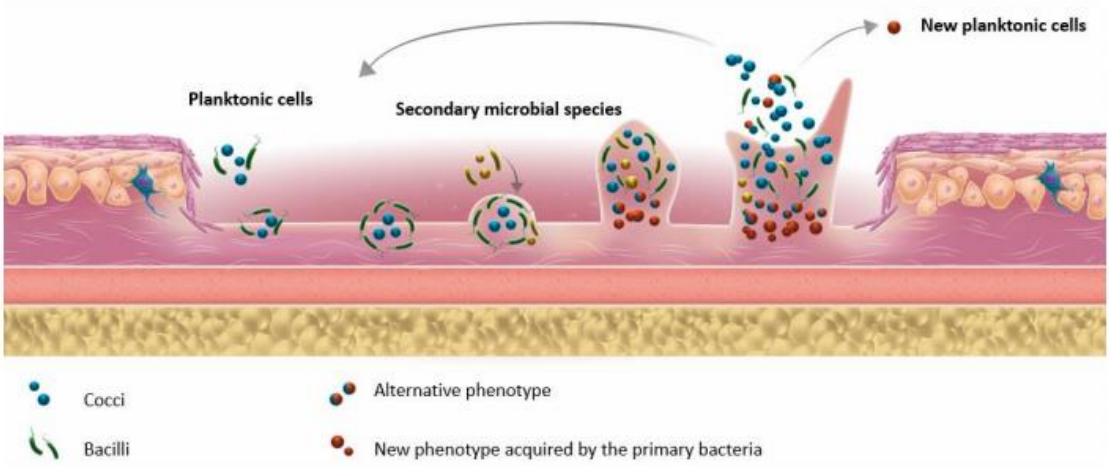

Figure 6: the steps of the formation of bacterial biofilm [33]

Neut and his coworker did a research in 2011 [34], they reached evidences that shows the biofilms in DFU using a certain techniques and microscopes, this finding was confirmed by Malik and his coworkers in 2013 [35] who study more than 170 DFU cases, and they found around 70% of the cases under studies suffers from DFI (Diabetic Food Infection).

In 2014, and 2015 Murali [36] and his coworkers, and Banu [37] and his coworkers, respectively, they support the findings of the previous research and

characterize and identify the S. aureus in the biofilms that present in DFU patients, this confirmation lead to a conclusion that prove the presence of bacteria in the biofilms that accompanied with chronic disease patients. Regarding the inhibition and the metabolism of the bacterial biofilms, the researchers end with the following conclusions:

- Using citrate and EDTA, the adhesion of the bacteria can be blocked; those are the most capable compounds due to their chelating properties.
- Natural compounds and complexes were used to achieve the inhibition to the biogenesis structures, these natural compounds are usually derived from plants.
- Adaptation and modulation is one of the important properties to the bacterial biofilms and colonies.
- Bacterial inhibition can be enhanced via the sessile bacterial kills, this can be done through dispersion the bacterial biofilm using enzymes or a certain compounds.

The entire above conclusion goaled to improve the therapy and develop the treatments against the bacterial biofilms and limited their activities toward chronic diseases.

REFERENCES

[1] Juhas M. Horizontal gene transfer in human pathogens. *Crit Rev Microbiol.* 2015. 41(1):101-8. doi: 10.3109/1040841X.2013.804031.
[2] Seitz P, Blokesch M. Cues and regulatory pathways involved in natural competence and transformation in pathogenic and environmental gram-negative bacteria. *FEMS Microbiol Rev*. 2013. **37**(3):336-63. doi: 10.1111/j.1574-6976.2012.00353.x.
[3] Nadell CD, Xavier JB, Foster KR. The Sociobiology of biofilms. *FEMS Microbiol Rev*. 2009. 33(1):206-24. doi: 10.1111/j.1574-6976.2008.00150.x.
[4] Savage VJ, Chopra I, and O'Neill AJ. Staphylococcus aureus biofilms promote horizontal transfer of antibiotic resistance. *Antimicrob Agents Chemother*. 2013. 57(4):1968-70. doi: 10.1128/AAC.02008-12.
[5] Liao J, Schurr MJ, and Sauer K. The MerR-like regulator BrlR confers biofilm tolerance by activating multidrug efflux pumps in Pseudomonas aeruginosa biofilms. *J Bacteriol*, 2013. 195(15): 3352-63. doi: 10.1128/JB.00318-13.
[6] Malik A, Mohammad Z, Ahmad J. The Diabetic foot infections: biofilms and antimicrobial resistance. *Diabetes Metab Syndr*. 2013. 7(2):101-7. doi: 10.1016/j.dsx.2013.02.006.
[7] Zhao G, Usui ML, Lippman SI, et al. Biofilms and Inflammation in Chronic Wounds. *Adv Wound Care (New Rochelle)*. 2013. 2(7):389-399. doi: 10.1089/wound.2012.0381.
[8] McInnes RL, Cullen BM, Hill KE, et al. Contrasting host immuno-inflammatory responses to bacterial challenge within venous and diabetic ulcers. *Wound Repair Regen.* 2014. 22(1):58-69. doi: 10.1111/wrr.12133.
[9] Veerachamy S, Yarlagadda T, Manivasagam G, Yarlagadda PK. Bacterial adherence and biofilm formation on medical implants: a review. *Proc Inst Mech Eng H*, 2014. 228(10): 1083-99. doi: 10.1177/0954411914556137.
[10] https://microbewiki.kenyon.edu/images/a/a7/Structuralbiofilm.gif
[11] https://www.wisegeek.com/what-is-an-anaerobic-infection.htm
[12] Dowd, S.E.; Wolcott, R.D.; Sun, Y.; McKeehan, T.; Smith, E.; Rhoads, D. Polymicrobial nature of chronic diabetic foot ulcer biofilm infections determined using bacterial tag encoded FLX amplicon pyrosequencing (bTEFAP). PLoS ONE 2008, 3, e3326.
[13] Park, S.; Rich, J.; Hanses, F.; Lee, J.C. Defects in innate immunity predispose C57BL/6J-Leprdb/Leprdb mice to infection by Staphylococcus aureus. Infect. Immun. 2009, 77, 1008–1014. [CrossRef]
[14] Ndosi, M.; Wright-Hughes, A.; Brown, S.; Backhouse, M.; Lipsky, B.A.; Bhogal, M.; Reynolds, C.; Vowden, P.; Jude, E.B.; Nixon, J.; et al. Prognosis of the infected diabetic foot ulcer: A 12-month prospective observational study. Diabet. Med. 2018, 35, 78–88.
[15] Lecube, A.; Pachón, G.; Petriz, J.; Hernández, C.; Simó, R. Phagocytic activity is impaired in type 2 diabetes mellitus and increases after metabolic improvement. PLoS ONE 2011, 6, e23366.
[16] Pereira, S.G.; Moura, J.; Carvalho, E.; Empadinhas, N. Microbiota of Chronic Diabetic Wounds: Ecology, Impact, and Potential for Innovative Treatment Strategies. Front. Microbiol. 2017, 8, 1791.
[17] Gardiner, M.; Vicaretti, M.; Sparks, J.; Bansal, S.; Bush, S.; Liu, M.; Darling, A.; Harry, E.; Burke, C.M. A longitudinal study of the diabetic skin and wound microbiome. PeerJ 2017, 5, e3543.
[18] Malone, M.; Johani, K.; Jensen, S.O.; Gosbell, I.B.; Dickson, H.G.; Hu, H.; Vickery, K. Next Generation DNA Sequencing of Tissues from Infected Diabetic Foot Ulcers. EBioMedicine 2017, 21, 142–149.
[19] MacDonald, A.; Brodell, J.D.; Daiss, J.L.; Schwarz, E.M.; Oh, I. Evidence of differential microbiomes in healing versus non-healing diabetic foot ulcers prior to and following foot salvage therapy. J. Orthop. Res. 2019, 37, 1596–1603. [CrossRef]
[20] https://courses.lumenlearning.com/microbiology/chapter/drug-resistance/
[21] https://www.niaid.nih.gov/research/antimicrobial-resistance-causes
[22] Wolcott, R.D.; Hanson, J.D.; Rees, E.J.; Koenig, L.D.; Philips, C.D.; Wolcott, R.A.; Cox, S.B.; White, J.S. Analysis of the chronic wound microbiota of 2,963 patients by 16S rDNA pyrosequencing. Wound Repair Regen. 2016, 24, 163–174.

[23] Jneid, J.; Cassir, N.; Schuldiner, S.; Jourdan, N.; Sotto, A.; Lavigne, J.P.; La Scola, B. Exploring the microbiota of diabetic foot infections with culturomics. Front. Cell Infect. Microbiol. 2018, 8, 282.
[24] Bowler, P.G.; Duerden, B.I.; Armstrong, D.G. Wound Microbiology and Associated Approaches to Wound Management. Clin. Microbiol. Rev. 2001, 14, 244–269.
[25] Oates, A.; Bowling, F.L.; Boulton, A.J.M.; McBain, A.J. Molecular and culture-based assessment of the microbial diversity of diabetic chronic foot wounds and contralateral skin sites. J. Clin. Microbiol. 2012, 50, 2263–2271.
[26] Gardner, S.E.; Hillis, S.L.; Heilmann, K.; Segre, J.A.; Grice, E.A. The neuropathic diabetic foot ulcer microbiome is associated with clinical factors. Diabetes 2013, 62, 923–930.
[27] Percival, S.L.; Malone, M.; Mayer, D.; Salisbury, A.M.; Schultz, G. Role of anaerobes in polymicrobial communities and biofilms complicating diabetic foot ulcers. Int. Wound J. 2018, 15, 776–782.
[28] Johnson, T.R.; Gómez, B.I.; McIntyre, M.K.; Dubick, M.A.; Christy, R.J.; Nicholson, S.E.; Burmeister, D.M. The Cutaneous Microbiome and Wounds: New Molecular Targets to Promote Wound Healing. Int. J. Mol. Sci. 2018, 19, 2699.
[29] https://www.nih.gov/news-events/nih-research-matters/preventing-bacterial-infections-medical-devices
[30] Yin, W.; Wang, Y.; Liu, L.; He, J. Biofilms: The microbial “protective clothing’ in extreme environments. Int. J. Mol. Sci. 2019, 20, 3423.
[31] Mottola, C.; Semedo-Lemsaddek, T.; Mendes, J.J.; Melo-Cristino, J.; Tavares, L.; Cavaco-Silva, P.; Oliveira, M. Molecular typing, virulence traits and antimicrobial resistance of diabetic foot staphylococci. J. Biomed. Sci 2016, 23, 33.
[32] Kumar, D.; Banerjee, T.; Chakravarty, J.; Singh, S.K.; Dwivedi, A.; Tilak, R. Identification, antifungal resistance profile, in vitro biofilm formation and ultrastructural characteristics of Candida species isolated from diabetic foot patients in Northern India. Indian J. Med. Microbiol. 2016, 34, 308–314.
[33] Pouget C , Dunyach-Remy C, Pantel A, Schuldiner S, Sotto A, et al. Biofilms in Diabetic Foot Ulcers: Significance and Clinical Relevance. Microorganisms 2020, 8, 1580; doi:10.3390/microorganisms8101580
[34] Neut, D.; Tijdens-Creusen, E.J.; Bulstra, S.K.; van der Mei, H.C.; Busscher, H.J. Biofilms in chronic diabetic foot ulcers—A study of 2 cases. Acta Orthop. 2011, 82, 383–385.
[35] Malik, A.; Mohammad, Z.; Ahmad, J. The diabetic foot infections: Biofilms and antimicrobial resistance. Diabetes Metab. Syndr. 2013, 7, 101–107. [CrossRef] [PubMed]
[36] Murali, T.S.; Kavitha, S.; Spoorthi, J.; Bhat, D.V.; Prasat, A.S.B.; Upton, Z.; Ramachandra, L.; Acharya, R.V.; Satyamoorthy, K. Characteristics of microbial drug resistance and its correlates in chronic diabetic foot ulcer infections. J. Med. Microbiol. 2014, 63, 1377–1385. [CrossRef]
[37] Banu, A.; Noorul Hassan, M.M.; Rajkumar, J.; Srinivasa, S. Spectrum of bacteria associated with diabetic foot ulcer and biofilm formation: A prospective study. Australas. Med. J. 2015, 8, 280–285. [CrossRef]
[38] Taha, O.A.; Connerton, P.L.; Connerton, I.F.; El-Shibiny, A. Bacteriophage ZCKP1: A potential treatment for Klebsiella pneumoniae isolated from diabetic foot patients. Front. Microbiol. 2018, 9, 2127.