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Bacterial Toxins and their Involvement in Generating Nanoparticles by Gram-positive bacteria

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Abstract: The emerging antimicrobial resistant pathogenic bacterial has led to the need to look into other therapeutic interventions like the use of nanomaterial which possess antimicrobial properties. This review is aimed at analysing the connection between bacterial toxins and nanoparticles generated by Gram-positive bacteria with regards to their practical use in the fight against Antimicrobial Resistance. For instance, Staphylococcus aureus and Bacillus cereus are gram-positive bacteria known to have multiple toxins that are capable of influencing its surrounding around cells. Current review has exposed some facts which reveal that it is involved in production of nanoparticles which have special effect against antibiotic bacteria. In the current review, the authors presents the ways through which bacterial toxins can trigger the creation of nanoparticles, properties of the created nanoparticles, and their probable applications in the generation of new antibacterial drugs. The treatment of infections has recently been compounded by the development of multidrug-resistant bacterial strains, thus calling for the development of measures that can help cope with infections. Nanotechnology mediated anti-microbial approaches such as using nanoparticles formed from bacterial toxins present a nascent way around this problem. These cases have made researchers to develop other mechanisms of eradicating bacterial infections other than the use of antibiotics, and nanotechnology is one mechanism that has attracted a lot of attention. Although the processes of nanoparticle formation using Gram-positive bacteria are still not clear, a number of investigations indicate that bacterial toxins can be essential for that. Bacterial toxins are extremely toxic compounds which are capable of profoundly affecting cellular processes and exerting a number of pathological consequences on the host organism.

Keywords: Gram-Positive Bacteria, Nanoparticles, Bacterial Toxins, Antimicrobial Applications

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1. Introduction

Introduction to Bacterial Toxins and Nanoparticles

Bacterial toxins are secreted by bacteria with the potential of causing harm to the human body. These toxins are mainly relevant with bacterial and other diseases that cause food poisoning. On the other hand, nanoparticles are largely defined as very small particles that have a size of between 1-100 nanometres and there has been a recent interest their use in fields like medicine, electronics and environmental uses [1-6]. These small particles have characteristics which make them suitable for sundry purposes [6-9]. Although in this nanoparticle, the presentation of bacterial toxins will be discussed, it is crucial to first mention the general background regarding bacteria, specifically gram-positive bacteria, which have features that differ from the Gram-negative [10]. The properties include; Peptidoglycan make up a thicker cell wall, smaller surface area/volume

ratio and teichoic acids in their cell wall which has so many functions in bacterial physiology, such as acting as a protection against phagocytosis[11]. Indeed, this paper aims at analyzing the relationships between several characters pertaining to gram-positive bacteria including the cell wall, teichoic acids and the averages between the production of toxins and nanoparticles[12]. The remarkable balance between bacterial toxins and the bio synthesis of nanoparticles by Gram positive bacteria is an area of interest that presents a lot of information on how opportune these microscopic organisms are and how ingenious they can be[13]. Effective and competent Gram-positive bacteria are well known from the standpoints of their explicit resistance and a number of the pathways of metabolism, which they utilize; additionally, they were primary objects of studying in the sphere of nanotechnology. Being a group of bacteria that possess a distinctive cell wall, these bacteria can produce various types of nanoparticles, which have applications in medicine, the environment, and other areas. In this process the interaction between a bacterium and its toxin, as well as the processes regulating the formation of these nanoparticles, appealing and rather paradoxical at the same time[14]. *Bacillus subtilis*, which is a gram positive bacterium, has exhibited a unique competency of synthesizing a plethora of nanoparticles that are made up of metals, metalloids and in some cases even organic compounds[15].

As such, this process is usually encouraged by the metabolic or even the path ways that these bacteria use to adapt to the environmental stimuli and shocks such as the presence of toxic compounds. It is worth to mention that bacterial toxins are synthesized as potent biomolecules, which are able to modulate and interfere with cellular functions of the host organisms and their production is effectively used by Gram-positive bacteria for nanoparticles manufacturing[16].

Gram-Positive Bacteria: An Overview

The group of gram-positive bacteria can be of various forms of developments such as *Streptococcus*, *Staphylococcus*, *Bacillus cereus* and so on. They can be distinguished by the chemical composition of their cell wall and the teichoic acids. These bacteria are thus important in the ecosystem and can either be harmless or pathogenic to man depending on the type and environment in which they are found[17-20].

Staphylococcus and *Bacillus* are examples of the gram positive group and they are known to synthesize several types of toxins that cause the derangement of host cell function and results in various diseases.[21] These bacteria also have the ability to produce overlapping secondary metabolites such as antimicrobial substances, peptide and lipopeptides [22].

2. Materials and Methods

The Relationship Between Bacterial Toxins and Nanoparticle Production

Maximizing scientific support, there presented information to the correlation between bacterial toxins and nanoparticles of Gram-positive bacteria[23]. Scientists have noted that some Gram-positive bacteria like *Bacillus* species are capable of synthesizing metal-based nanoparticles due to the happens metabolic activities[24].

It is possible that these nano-particles can show moderate to high level of antibacterial activity due to their capability to cause direct damage to bacterial membranes and cell wall, invade the bacterial cytoplasm and alter the internal metabolic processes and induce the generation of Reactive oxygen species(ROS)[25].

These toxins are excreted as proteins they may be directly or indirectly lethal to bacteria present in the body. Such toxin is the pore-forming toxin synthesized by *Streptococcus pyogenes* that causes an alteration of host cell membrane integrity and leads to cell death. The *Staphylococcus aureus* for instance produces exotoxins that are associated with skin infections, food poisoning, and toxic shock syndrome[26].

These toxins can also be used to synthesize nanoparticles which are increasingly being sought after in the various fields such as in drug delivery, catalysis and electronics. Thus, it can be stated that the connection between bacterial toxins and nanoparticles synthesis has not been investigated comprehensively yet[27].

3. Results and Discussion

The Role of Cell Wall Structure in Nanoparticle Interactions

Due to the thick layer of peptidoglycan a direct interaction with synthesis of the nanoparticles is possible. This structural feature provides a direct access of the bacterial cell to the external environment and for the ability to collect substances, such as metal ions and other precursors needed for formation of nanoparticles. Moreover, the outside surface charge and hydrophobicity of the Gram-positive cell wall can affect nanoparticles adsorption and interaction, while the change of these properties can affect the nanoparticles' physiochemical performances and their biological roles[28].

Because the cell wall of Gram-positive bacteria comprises a thick layer of peptidoglycan, these bacteria are central to metal-based nanoparticle interactions.[21, 24].

This is because the negatively charged functional groups found at the surface of the bacterial cell can cause strong electrostatic attraction with the nanoparticles and thus alter the cell membrane permeability which is likely to lead to cell damage or death [21].

Also, rough surface morphology of some NPs may increase dissolution rate and local ion concentration which is also helpful in antibacterial activity of NPs[24].

Synthesis of nanoparticles by Gram positive bacteria appears to be intricate and a systems level process, which may include bacterial toxins the total architecture of bacterial cell wall and metabolism of these bacteria[29].

Mechanisms of Nanoparticle Production By Gram-Positive Bacteria

It is very important to mention that the synthesis of nanoparticles by Gram-positive bacteria entails several processes at the cellular level and diverse metabolic pathways. One of the key mechanisms is the decrease of metal ions by enzymes of bacteria or other reducers, for example, reducers that are present in the bacterial electron transport chain. Such a process, which may be induced by bacterial toxins, may result in the formation and development of nanoparticles either within bacterial cells or in the surroundings[21]. Besides, the metal reduction the fundamental characteristic, the bacteria have been also reported to form nanoparticles via the synthesis of biomolecules like, proteins and polysaccharides that act as capping or stabilizing agents controlling size, shape and other physical and chemical property of the formed nanoparticles[30].

The involvement of bacterial toxins in this process is rather ambiguous since they can affect the cellular sensitivity to the presence of metal ions or other nanoparticle precursors, stimulating the beginning of certain metabolic path.[31]. strategies or the overexpression of genes that are related to nanoparticle manufacture[32].

It may be concluded that the mechanisms of nanoparticle formation by Gram-positive bacteria seems to be a manifold and intricate process, which could involve bacterial toxins, changes in the cell wall composition and the metabolic versatility of these organisms[29].

Some observations made by researchers have realized that some of the Gram-positive bacteria for instance *Bacillus* species are capable of synthesizing metal based nanoparticles through their metabolic activities. These nanoparticles can show remarkable antimicrobial activity, perhaps due to membrane damage by the nanoparticles, disturbance of normal cell processes and generation of oxidative stress[33].

The aspect of the cell structure that is most significant for the Gram-positive bacteria and their reactions towards metal-based nanoparticles is the thickness of the peptidoglycan layer in the cell wall. The negatively charged functional groups existing on

the bacterial cell surface can be adsorbed by the nanoparticles through electrostatic interactions; these changes cause the permeability of the cell membrane and may lead to cell damage or death[34].

Bacillus subtilis has been known to be efficient in the synthesis of Nanoparticles due to its efficiency in the synthesis of biomaterials like biofilm and extracellular polymers. The formation of nanoparticles in these bacteria can be done through various routes, and one of these is through the bacterial toxins[35].

It has also been identified that one of the most frequent methods of nanoparticle fabrication by Gram-positive bacteria involves the use of enzymes. These enzymes can catalyze the oxidation of organic molecules into such inorganic ions as the metal ions which can in turn be used in formation of nanoparticles. For instance, certain species of bacteria, for example, *Shewanella* and *Pseudomonas* secrete potassium-reducing enzymes for the reduction of metal ions to the elemental state. In the case of *Bacillus subtilis*, enzymes like NADH dehydrogenase are involved in the synthesis of nanoparticles by bring Metal ions to their elemental state. Further, *Bacillus subtilis* has also been reported to generate nanoparticles by using the enzymes such as super oxide dismutase, catalase and hydrogen peroxide reductase[36].

Also, there has been an indication that bacterial toxins are capable of impacting on the synthesis procedure of nanoparticles by Gram-positive bacteria. The mechanisms of bacterial toxins effecting the production of nanoparticles by gram-positive bacteria are as follows[37].

Impact of Bacterial Toxins Nanoparticle Properties

Recent results showing the involvement of Gram-positive bacteria in the synthesis of nanoparticles and an association of bacterial toxins synthesis. Different studies have also shown that bacteria which belong to the Gram-positive group like *Bacillus* species is capable of synthesizing metal based nanoparticles as a byproduct of their metabolisms. These nanoparticles can contain significant antibacterial activity, possibly due to their membrane damaging, cell homeostasis disturbing, and ROS producing effects.[28, 38].

Several mechanisms for nanoparticle creation by Gram-positive bacteria may exist because of the complexity of the process and bacterial toxins, cells, and the metabolism of many of these bacteria. For example, Gram-positive bacteria can attach to the surface of the nanoparticles depending on the charge they possess which causes alteration of membrane permeability and cell death or inactivation[21].

Also, the nano structures such as irregular surface topology of some nanoparticles may also increase the dissolution rate and ion concentration of the nanoparticles which plays a role in antimicrobial activity[23].

The investigation of potential link between bacterial toxins and nanoparticles synthesized by gram positive bacteria can have a great prospect towards evolution of new idea in antimicrobial approach. The genera *Staphylococcus* and *Bacillus* are examples of Gram-positive bacteria, these bacteria have a unique ability to produce secondary metabolites including; antibiotics, peptides and lipopeptide[39].

Till date, it has been discovered that bacterial toxins belonging to several Gram-positive bacterium are significantly involved in the synthesis and properties of nanoparticles. These toxins which can interfere with cellular functions and cause oxidative stress seem to initiate or coordinate the processes through which the Gram-positive bacteria fabricate nanoparticles[39].

For example, the presence of bacterial toxins such as hydrogen peroxide might increase the formation of reactive oxygen species leading to redox catalytic synthesis of metal or metal oxide nanoparticles[40]. Moreover, it was also pointed out that the inability to determine the precise location where nanoparticles are formed, which is usually associated with the bacterial cell wall and membrane, may be determined by the view of

the interaction between the toxins and other cellular components. Thus the attributes of the resulting nanoparticles include size, shape and surface characteristics may be altered by the presence of bacterial toxins. Such alterations in the characteristics of the nanoparticles by these toxins can also affect their antimicrobial properties, thus, either increasing or decreasing the bactericidal properties of the nanoparticles[41].

Prevention and Treatment of Bacterial Toxins Contamination

Thus, the ability of nanoparticles synthesized by Gram-positive bacteria, which may be regulated by toxins, presents novel prospects for the creation of new antimicrobials. Some specialists have mentioned that *Bacillus* species and a number of other Gram-positive bacteria can produce these nanoparticles. These nanoparticles can act as a significant antimicrobial agent and can affect bacterial cell membranes leading to the perturbation of the cell homeostasis and ROS production metal-based nanoparticles due to their metabolic activities[28, 38].

The outer layer, peptidoglycan layer in bacteria particularly in Gram-positive bacteria, is highly responsible for their interaction with the metal based nanoparticles. The functional groups that have a negative charge can get attached to the bacterial surface through electrostatic interaction to the nanoparticles and hence alter the permeability of the cell membrane and consequently lead to cell damage or even cell death. Also, due to the high surface roughness of some of the particles, their dissolution rate and ion release at specific area may also increase, which also contribute to the antimicrobial activity [38].

Secreted bacterial toxins are dangerous for humans since the impacts may vary from simple foodborne illness to critical diseases.

In this regard the prevention and treatment of bacterial toxins contamination is of paramount importance in the general health of the public. Some key strategies include [42]:

1. Proper food handling and storage: Avoiding the mishandling and cross-contamination of food especially when preparing barbecues, salads and other perishable foods can go a long way in the reduction of toxin producing bacteria.
2. Effective cleaning and disinfection: Once again, nasty bacteria often multiply and spread on surfaces, equipment and even facilities, therefore, new methods to harmfully clean them are recommended to utilize.
3. Early detection and rapid response: One way of reducing the high probabilities of bacterial toxin related outbreak is to enhance monitoring and surveillance frameworks that can detect any such problems early enough. Present day innovations in the area of nanotechnology are expected to proffer practicable means to the problem of bacterial toxins.

Applications of Nanoparticles Produced By Gram-Positive Bacteria

Thus, the fact that Gram-positive bacteria are capable of generating antimicrobial nanoparticles arising from the production of toxins broadens the prospects for the creation of novel antimicrobial approaches. These nanoparticles can be utilized in a variety of applications, including: The prospective applications of Quorum sensing inhibitors are in new antimicrobial agent development, in the management of infected bacterial infections, and the inhibition of biofilm formation, as well as in wound healing processes[43].

Scientists have noted, that nanoparticles, synthesized by Gram-positive bacteria could have a high pathogen unwanted organism killing capacity targeting both Gram-positive and Gram-negative bacteria and multidrug resistant strains. [44]Some of the characteristics of nanoparticles include; a high relative surface area and high ability to penetrate through bacterial cell membranes, which is a highly significant in eliminating antimicrobial activity[45].

In addition, the nanoparticles produced by the Gram positive bacteria have been reported to exhibit anti-biofilm potential because they prevent the formation of biofilms that are considered more resistant to antibiotics treatments[46].

Further, the multiplicative actions of nanoparticles combined with other antimicrobial agents have been studied in order to develop other uses of these biogenic nanoparticles. In this way, if researchers comprehend exactly the ways through which Gram-positive bacteria devise these nanoparticles, then they are able to improve the generation of these particles and also modify their characteristics to effectively respond to certain antimicrobial problems[47]. Contribute to the creation of new modalities of antimicrobial therapy that can combat a broad spectrum of bacterial organisms inclusive of the resistant ones[48].

Recently, self-assembled nanoparticles synthesized by gram positive bacteria have attracted much attention comparatively in virtue of their multifaceted utilization in medical, electronics, and environmental science divisions. Here are some of the notable applications of these nanoparticles [49]:

- a. **Medicine:** The nanoparticles synthesized by the gram-positive bacteria have proved to be highly beneficial in the medical field especially in the treatment through drug carriers. Thus, with the help of these nanoparticles, researchers were able to enhance solubility, bioavailability and target specificity of various therapeutic agents. For instance, some scientists have been able to apply nanoparticles from *Staphylococcus aureus* for delivering anticancer drugs to the target site, with a reduction in generalized effects and enhancement of the treatment's effectiveness. Furthermore, these nanoparticles work as medical diagnostic imaging agents; better diagnosis and tracking of diseases in the human body are made possible.
- b. **Electronics:** The particles which are made of bacterial materials have also been used in electronics industry to help in making sensors, transistors, and other electronics. These nanoparticles can be employed in conductive applications better than other conductive materials through the provision of superior conductivity. The versatility of these nanoparticles has been attributed to the features like self-assembling and biocompatibility; this has created different electronic devices which include OLEDs, TFTs, and organic memory.

Future Perspectives and Research Directions

The correlation of bacterial toxins and nanoparticles synthesized by the Gram-positive bacteria are a topic of research interests, and their prospects can be implemented in medicine, agriculture, and in environmental engineering. Further research pertaining to this relationship should be conducted in a bid to enhance the generation of these nanoparticles and fully explore all the possibilities for utilization[50].

It is also necessary to discuss the influence of bacterial toxins on the characteristics of the resulting nanoparticles as well. For instance, the presence of bacterial toxins that inducible by the nanoparticles can affect size, shape, composition as well as surface characteristics of the nanoparticles. [10]This can in turn alter the effectiveness of the nanoparticles in different uses or functions that they are put to. Thus, it is possible to continue the experiment to elucidate the role of bacterial toxins to define the properties of nanoparticles.[10].

At the same time, the identification of new classes of bacterial toxins will contribute to progress in the synthesis of nanoparticles. Scholars have in the recent past identified new molecules created by Gram-positive bacteria that have distinctive features[51].

From these new toxins one may infer that they can be used as the basis of description of the nanoparticles that will have advanced characteristics. For example, through employing bacterial toxins as molds, one can synthesize nanoparticles of precise size and shape. This can in turn result in the discovery of new methods of delivering drugs and vaccines, creation of biosensors and other uses in biotechnology and the medical field. [52].

In addition, the study of bacterial toxins and nanoparticles make advances in arresting and counteracting methods [52].

Thus, the interactions of bacterial toxins with the synthesis of nanoparticles by Gram-positive bacteria create great opportunities for future research and uses. Therefore, by expounding on the ways that these toxins affect the synthesis and properties of nanoparticles, researchers can possibly translate this information into enhanced antimicrobial methods, and innovative concepts of purification[53].

4. Conclusion

Studies of toxic substances in bacterial infections and the production of nanoparticles by Gram-positive bacteria are a rather vast and interesting direction of research. The present review has emphasized on the contribution of cellular structure of the Gram-positive bacteria in controlling the interactions and synthesis of the nanoparticles and the effects that bacterial toxins might have endured on the properties and the functionality of the nanoparticles.

The further development of the nanotechnology means that the deeper insight into the processes occurring between toxins and nanoparticles in relation to the gram-positive bacteria will be crucial to exploitation of new materials embedded in this area. The further studies should be devoted to explaining how bacterial toxins affect the intracellular signaling and metabolic networks and, in consequence, the formation of nanoparticles and their properties. Also, further research on the possibilities of employing the resulting toxin-sensitive nanoparticles in the fields of antimicrobial chemotherapy, environmental treatment, and biomedical engineering will be important. Thus, scholars willing to perform the link between the complex domain of bacterial toxicology and the highly prospective area of nanotechnology can open the door to the discovery of better, target-oriented, and more sustainable solutions to some of the most crucial problems. Through applying the conclusions of this research, it is possible to outline the further path to creation of the more efficient and stable development solutions for the pharmaceutical and biotechnological sectors as well as for the problems of environmental protection, which are topical globally. Based on the findings of this study, it is possible to define the further path in searching for new approaches to the creation of more effective and more stably oriented development solutions within the spheres of drug production.

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