ABSTRACT
Surface layer as the outer protective coverage of bacteria and archaea are two-dimensional crystalline and symmetrical arrays of proteins that recently attract a lot of attention for biologist scientists. The surface layers of bacteria are usually 5 to 10 nm in diameter and represent highly porous protein lattices with uniform size and morphology with the pore sizes of 2 to 8 nm. The crucial and most prominent property of this protein-based layer is the regular morphology and suitable chemical composition for different biological applications. Although the formation mechanism of surface layers is different from one type of cell to another once, the surface layer protein molecular compositions almost are same for all types. Recently, the biological application of surface layers opens a prominent research fields in surface biological science such as nano-biotechnology adhesion, vaccination, pharmaceutical, biosensors, bioremediation and mineralization application. In this mini review, we discussed about the main application of this nano-layer in biological systems.

Key words: biosensors, bioremediation, bacteria, pharmaceutical application, Surface layer

INTRODUCTION
During the evolution process, one of the most prominent factors that led some microorganisms to survive in harsh environmental conditions was to equip themselves with a series of superficial outer surface layers. In amon of various types of microorganism, the prokaryotic cells were the first group of cells that could equipped outer their own surface layers [1]. Today, all of biologists agree with each other that the surface layers are the single proteinaceous layer [2]. These layers are the two-dimensional proteinaceous surface that these layers often are the protective application for cells. Principally, although surface layers proteins almostly involves the ten percent of total constructive proteins of cells; we can call these proteins as main and major source of biopolymers [3]. Up to now, researchers have earned the essential morphological, physiochemical information about the surface layers. Nerveless, the more biological application of surface layers almostly have been in a state of ambiguity. In Archaea cells as one of oldest type of cells [2,4], the surface layer has a crucial and prominent role in cell shape[5]. As respected to this fact that, the surface layer protein is synthesis by the cell and it’s possible to changing the protein chemical composition by genetic manipulation. According to this fact that, recently, the particular patterns and arrays of supramolecular layer such as proteins, nucleic acids have been reported [6]. From molecular prospective, depending on the bacteria type the surface layers have different structures. At least, Gram-negative types have been attached on lipid membrane layer of cell...
wall, while the Gram-positive types have been bound to the rigid peptidoglycan-containing layer via secondary cell wall polymer [7]. Of course, some types of cells surface layers have been formed from double layers of different proteins. Recently, for exact consideration of surface layers, the scanning electron microscopy, electron crystallography, X-ray and neutron scattering techniques have been used for morphological and molecular detections of surface layers [8]. Many of morphologic studies of surface layers indicated this fact that, the surface layer proteins make the symmetrical patterns [4]. Exactly, the symmetrical patterns have regular nanometric scale shapes such as oblique, hexagonal and square shapes and so on with center-to-center spacing of the morphological units of 4–35 nm. Surface layers of bacteria represent highly porous protein lattices with uniform size and morphology in the range of 2–8 nm. Bacterial surface layer diameter is usually 5–10 nm, whereas archaea surface layers frequently exhibit a much thicker than bacteria. These surface layers proteins arrays were shown in Fig 1[9]. hexagonal morphologies of surface layers proteins [9].

The symmetrical patterns of surface layers make it possible to proteins have a lateral interaction. Of course, the surface layers interaction by interlayers are almostely stronger than lateral once. The almostely weak lateral interactions of proteins make it possible for proteins to have a suitable changing of their patterns in cell division process [10]. In recent decades, chemical experiments about the surface layers indicated that, almostely the surface layers have been formed from the same proteins with different molecular mass range from 40-170kDa [11]. The exact consideration and studies exhibited that, mostly the hydrophobic acidic proteins and glycolic proteins are the main ingredients of surface layers [12]. Recently, as an in vivo assembly of surface layer, excessive synthesis of proteins main builders and dynamic transformation to outer part of cells are the crucial parameter for defect-free surface layer forming. According to this issue, the surface layer synthesis process strictly adjusted by proteins transformation [13]. From the mechanistic point of view, the different Gram-negative and Gram-positive bacteria choose the different mechanism for surface layer fabrication and development.

Fig 1. (A) The schematic architecture of bacterial and archaea surface layers (B) The Oblique, square and hexagonal morphologies of surface layers proteins [9]
The more research about this issue indicated that, the Gram-positive bacteria start to produce the multiple and cylindrical shaped surface layer bands, while the Gram-negative types develop the surface layer by creating new subunits of surface layers. According to mention above, the surface layers as a protective coverage layer can influence to cell shape and division process that the Archaea cell is one of the best examples for this point [14]. Moreover, the glycosylated proteins in surface layers can be formed the various interactions by surrounded media such as hydrophilic and hydrophobic interactions [15]. For measuring of this interaction, the contact angle techniques can help to study the hydrophilic and hydrophobic interaction of surface layers as one of the best methods [16]. Last decades scientific consideration results indicated that, the surface layers with unique surface properties have high potential for various application in different biological and medial scientific fields. In addition to nanotechnological application of surface layers, in recent scientific reports the antifouling, exoenzymatic, vaccination and adhesive application of surface layers have been studied [17].

**Biological Applications**

**Adhesive application of surface layers**

One of the best application of surface layers are the improving the bacterial adhesion that this field take the more attention of biologists. According to this fact that, the surface layers are the key role in adhesion. So, Kos et al, considered the Lactobacillus based surface layers for porcine ileal epithelial cells adhesion. Their results indicated that the surface layer have a crucial role in cells adhesion. To ensure of surface layer effect on adhesin force, the removal and extraction test of surface layer indicated the reducing in autoaggregation of cells. So, the Lactobacillus based surface layers have a positive effect in adhesion force of cells [18]. In another study, Johnson et al reported the adhesive effect of surface layer of Lactobacillus acidophilus NCFM on Caco-2 intestinal epithelial cells in vitro. Their results showed that in addition to adhesive effect, the modulation of dendritic cells was another positive effect of surface layers [19].

**Application of surface layers in vaccination**

In the last decades, the immunization process is one of the most important steps of vaccine production, which the surface layer fusion proteins have critical role in that. Therefore, in various types of surface layers, the Lactobacillus based surface layers have been suitable candidate for this application. The suitable immune and good antigen expression process are the strength point of Lactobacillus based surface layers for immunization. So, the surface layers have remarkable activation effect of immune system. As a mechanistic prospective for this crucial role, Ausiello et al proposed that the surface layers have a stimulated effect on more secretion of inflammatory cytokines and dendritic cells [20,21].

**Pharmaceutical application of surface layers**

Surface layers with unique properties are good candidates for supporting the liposomes for pharmaceutical application. According to this issue, the surface layers can form the regular crystalline patterns on liposome. Many of reports about this issue have been concentrated on the different possible interactions of surface layers proteins and liposome surface. Most of results indicated that the surface layers have been able to form the cross-link and covalent bonds by liposome surfaces [22]. Although the liposome supported surface layers could to from the single protein layer, this single layer does not have any effect on liposome shape. As a one of pharmaceutical application of surface layers, the liposome supported surface layers can enhance the mechanical stability of biologically active biomolecules. Mader et al, reported the liposome supported the crystalline surface layers. They reported the functional surface layers for entrapping of target biomolecules [23]. Therefore, the surface layers support liposome has high potential for crucial and important drug delivery and gene therapy applications [21].

**Application of surface layers in biosensors**

The immobilization of biomolecules on different surfaces are the one of challenge in biological science. The solving of these problem can be possible by using the nano-surface layers proteins. According to this issue, the microarray of DNA can be formed on surface layers efficiently. The carboxylic acid functional groups make it possible that the DNA and another type of biomolecules immobilized on surface layers regular and periodically. So, the surface layers can be used as an immobilizer for biomolecular sensors. As mention above, Scheicher et al
developed the microarray of DNA on surface layer for biosensor applications. Their results indicated that, the microarray of DNA can be formed on surface layer. These surface layers make possible the immobilization and detection of complex biomolecules such as DNA [24].

**Bioremediation and mineralization application of surface layers**

In addition to mention above application of surface layers, the ecological roles of bacterial surface layers are very interesting and important. For example, the surface layer of Synechococcus bacteria can stimulate the mineralization process of calcium carbonate. Principally, symmetric regular surface layers can influence on nucleation process [25]. Recently the biominalerization of inorganic materials on surface layers have attract a lot of attention of biologists. The biominalerization process on surface layers is an efficient method for increasing the catalysts and scaffolds-based materials. According to reports, different surface morphology of surface layers can be caused to various nucleation pathways. Consequently, the final scaffolds and catalysts that have been fabricated by surface layer technique, mineralized in surface layers template shapes [26].

So, the surface layers can enhance the mechanical strength, specific surface area and suitable morphology of catalysts and scaffolds-based materials. In addition to these issues, the surface layer is good candidate for bioremediation of heavy metals such as uranium wastes. Briefly, the surface layers proteins can to entrap the uranium ions and remove their waste from environment aqueous ecology. Therefore, the environmental friendly application of surface layers is the one of industrial and critical issues for biologists that recently attracts a lot of attention of many researchers [27].

**CONCLUSION**

The morphological and protein-based composition of surface layers have a different application in biological science in last decades. The best and critical properties that have a remarkable role in their application is symmetrical and regular proteins arrays. These properties solve the many of restrictions in different fields for biologists. Enhancing the adhesion of cells, induced effect in vaccination, increasing the mechanical stability of liposomes, strengthening of immobilization of biomolecules and changing of nucleation process of inorganic materials for fabrication of efficient medical therapy materials are the best advantages of surface layers that discussed in this review. So, the surface layers can be a good candidate for different biological applications.

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**CONFLICT OF INTEREST**

The authors declare that they have no conflicts of interest.

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