Bacterial contamination and biofilm formation on abiotic surfaces and strategies to overcome their persistence

S.O. Khelissa 1, 2, M. Abdallah 2, C. Jama 1, C. Faille 2, N-E Chihib 2,*

1 Université de Lille 1, CNRS, ENSCL, UMR 8207-UMET-PSI, Avenue Dimitri Mendeleiev, CS 90108 59652 Villeneuve d’Ascq, France
2 Université de Lille 1, CNRA, UMR 8207-UMET-PHIM, 369 rue Jules Guesde, CS 20039, 59651 Villeneuve d’Ascq, France

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Abstract
Abiotic surfaces are vulnerable to bacterial adhesion and to biofilm formation. Therefore, it is necessary to understand the parameters that influence bacterial adhesion to find out solutions against cell adhesion and biofilm formation. The ability of pathogenic bacteria to adhere and to form biofilms on abiotic surfaces represents a major health safety problem. Bacteria embedded in biofilms are more resistant to sanitizing agents than those growing under planktonic state. In fact, surface contamination by these pathogens is enhanced by favorable environmental conditions encountered in food and health sectors. Thus, the understanding of bacterial adhesion and biofilm formation on abiotic surfaces is of interest to setup efficient anti-biofilm strategies. In this context, this review highlights the main factors controlling the bacterial adhesion and biofilm formation on abiotic surfaces. It also describes the current and emergent strategies used to eradicate and prevent the biofilm formation on the most frequently used abiotic surface.

1. Introduction
Microbial adhesion onto abiotic surfaces and therefore the biofilm formation are considered serious issues, regarding their economical and public health consequences in many sectors, such as food-processing and healthcare ones. The presence of pathogenic microorganisms on food sector facilities represents a severe potential health risk to consumers. Contaminated food contact surfaces promote contamination of food products which leads to Food-Borne Diseases (FBDs) [1]. In 2014, 864 FBD outbreaks were reported in the United States (US) resulting in 13,246 illnesses, 712 hospitalizations, 21 deaths, and 21 food recalls [2].
According to the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC), a total of 5,251 food-borne outbreaks, including water-borne outbreaks, were reported in the European Union (EU) in 2014. Overall, 45,665 human cases, 6,438 hospitalizations and 27 deaths were reported. The evidence supporting the link between human cases and food vehicles was strong in 592 outbreaks [3]. In healthcare sector, orthopedic implant surface bacterial contamination is responsible for nosocomial infections also called Healthcare-Associated Infections (HAIs). Such infections are defined as infections that occurred during a hospitalization and are not present prior to hospital admission. Generally, nosocomial infections appear after prosthetic and implant surgery by handling contaminated or non-sterile devices. In France, from 1999 to 2006, 14,845 surgical site infections were reported involving 964,128 patients in 838 participating hospitals [4]. HAIs and FBDs are responsible for high critical economic losses. In fact, the direct cost of the HAIs was up to $16.6 billion in the US hospitals [5]. It has been reported that the resulting aggregated annual cost of FBD was $77.7 billion [6]. Generally, microorganisms live attached to surfaces and form biofilm [7]. When bacteria grow within a biofilm they gain several advantages, including enhanced resistance to antimicrobial agents [8]. Biofilms represent a threat to public health when found in food [9] and medical sector [10]. In addition, biofilms are also of concern in different other sectors such as maritime...
environment [11], water systems [12] and in oil pipes industries [13]. Their formation results in heavy costs in cleaning and maintenance. The persistence of biofilm in both food and medical sectors may constitute a reservoir for pathogens which increase the occurrence of HAIs and FBDs. Therefore, it is necessary to investigate different strategies in order to reduce the bacterial adhesion and the formation of biofilm. Disinfection is an important used strategy to control biofilm formation and to avoid infection transmission. Other strategy requires designing abiotic surfaces able to hamper the bacterial adhesion and therefore the biofilm formation.

Rather than developing new materials, another promising way is surface modification of existing surfaces [14] by grafting functional chemical groups or antibacterial molecules inhibiting bacterial adhesion [15]. However, the main challenge here is the durability of the treated surface [16]. Thus, setting up antimicrobial surfaces could be very useful for food processing equipment to enhance the food safety and in biomedical sector to prevent microbial colonization on hospital surfaces. To achieve such challenge, the choice of appropriate antimicrobial molecules and surface modification techniques is required. In addition, a deep understanding of the interaction between three main components: the bacterial cell, the attachment surface, and the environmental parameters is needed. In this regard, the goal of this review is to discuss the impact of bacterial adhesion and biofilm formation on abiotic surfaces. In addition, we attempt to highlight the strategies and approaches commonly applied in order to prevent bacterial adhesion and by the way biofilm formation.

2. Main pathogenic bacteria associated with FBDs and HAIs

2.1. Food-borne diseases

Bacteria are all around us, in the air, on surfaces and in/on the human body. Bacteria are often harmless but some of them can be pathogenic for humans. In natural, industrial, hospital and domestic environments, there are many persistent pathogenic bacteria such as Listeria monocytogenes, Staphylococcus aureus, Salmonella spp., Escherichia coli, Pseudomonas aeruginosa and Bacillus cereus which have serious economical and public health consequences. The contamination of abiotic surfaces with these pathogens leads to human infections worldwide [17]. L. monocytogenes has been involved as causative agent of FBDs due to its ubiquitous nature and its ability to grow under hostile conditions [18,19]. This bacterium is frequently associated with FBDs outbreaks that are characterized by wide spread distribution and relatively high mortality rates. Listeriosis, a serious infection, is usually caused by eating contaminated food. The disease primarily affects older adults, pregnant women, newborns, and adults with weakened immune systems. According to the EFSA and the ECDC, the number of confirmed human listeriosis cases in the EU increased slightly to 1,642 in 2012 compared with 2011 [20]. This number includes 198 death cases, which represents the highest number of fatal cases reported since 2006. According to this study, France is the most affected country with up to 63 fatal reported cases. Thus, the EU fatality case rate was 17.8 % among the 1,112 confirmed cases (67.7 % of all confirmed cases) [20]. The CDC estimates that about 1,600 illnesses and 260 death cases due to listeriosis occur annually in the US [21]. The worst listeriosis outbreak in the US history has occurred in 2011 and it was associated with consumption of cantaloupe from a single farm. In fact, 147 illnesses, 33 deaths, and 1 miscarriage were reported in 28 states [22]. This psychotrophic microorganism is able to grow at refrigeration temperatures as low as 2 to 4°C [23] and to contaminate the food-processing environment. Contamination of food with L. monocytogenes seems to occur most frequently during the food-processing due to the ability of this bacterium to attach to Stainless Steel (SS) and other abiotic surfaces [24] and form biofilm [25]. In addition, L. monocytogenes has been isolated from various surfaces in dairy and meat processing environments [26]. FBDs are also commonly caused by Gram-positive enterotoxigenic S. aureus [27]. S. aureus is an ubiquitous bacterium which can be found in the air, dust, sewage, humans and animals. In France, food poisoning cases associated with S. aureus have been listed in 2012 as the first cause of food-borne outbreaks [28]. In fact, 300 of 1,288 reported food-borne outbreaks (23%) were due to this pathogen [28]. S. aureus is able to adhere and form biofilm in food processing plants [29]. Despite the inactivation of S. aureus by heating the food prior to consumption, this bacterium can still induce intoxication. In fact, staphylococcal enterotoxins remain stable since they resist to extreme environmental conditions (freezing, drying, heat treatment, low pH and proteolytic enzymes) [27,30,31]. According to the EFSA and ECDC [32], in 2011, 6.1 % of all food-borne outbreaks in the EU were caused by staphylococcal toxins. This represent an increase of 25.9 % compared to 2010 (274 outbreaks) and was mainly due to the fact that France has reported 290 outbreaks in 2011 compared with 220 in 2010. In France, S. aureus represents the second cause of FBDs after Salmonella with 1,361 cases [33]. Salmonella spp. is the major food-borne pathogen for humans and animals worldwide. It has been reported that about 1.4 million human salmonellosis cases occur in the US leading to more than 16,000 hospitalizations with nearly 600 deaths and resulting in a high cost amounting to several billion dollars annually [34]. In 2012, the number of
salmonellosis cases in humans decreased by 4.7% compared with 2011. A statistically significant decreasing trend in the EU was observed over the period 2008-2012. A total of 91,034 confirmed human salmonellosis cases were reported in 2012 [20]. The two most common Salmonella serovars, involved in food poisoning outbreaks, are Typhimurium and Enteritidis [35]. Salmonella Enteritidis was the predominant serovar associated with the Salmonella outbreaks accounting for 66 % of human cases involved in these outbreaks followed by Salmonella Typhimurium which has been associated with 16.9 % of cases. The persistence of Salmonella in food processing environment, despite the cleaning procedures, could lead to microbial cross-contamination and to biofilm formation [36,37]. In fact, several studies have demonstrated the ability of Salmonella to form biofilms on abiotic surfaces such as SS [38], plastic [39] and rubber [40]. Generally, once attached, these pathogens may produce resistant biofilms constituting a reservoir for cells which, once detached, contaminate food products continuously. In addition, it is now established that in natural and man-made ecosystems, more than 99.9% of micro-organisms live attached to surfaces and form a specific and complex structure called biofilm. E. coli strains are common bacteria of the gastrointestinal tract [41]. Some E. coli strains are able to produce toxins that induce serious human infections [41]. Grass-fed cattle are the main reservoir of such E. coli strains. Their faeces might contaminate the meat during slaughter and thus act like microbial carrier which might end up contaminating other foods (e.g. milk, vegetables) and water. Outbreaks due to E. coli 0157:H7 have been associated primarily with consumption of undercooked beef meat, but also other foods have been involved as contamination carrier [42]. In fact, cross-contamination of foods can occur in food-processing plants and during subsequent handling and preparation, resulting in a wide range of foods being involved in E. coli 0157:H7 outbreaks [43,44]. In 2011, the ECDC have reported 2,495 food-borne outbreaks caused by the pathogenic E. coli including 54 deaths in the EU [32].

2.2. Nosocomial infections

According to the ECDC the most frequently reported HAI type was pneumonia and other lower respiratory tract infections, representing 25.7% of all reported HAIs [45]. The second most frequently reported type of HAI was surgical site infection (18.9%) followed by urinary tract infection (17.2%), bloodstream infection (14.2%) and gastro-intestinal infection (7.8%) [45]. S. aureus and P. aeruginosa are in the top four microorganisms most frequently isolated from these HAIs in the EU [45]. P. aeruginosa is found in various environmental niches including soil, water, plants, and hospital environments [46]. Despite the advances in health care and the improvement of strict disinfection procedures, P. aeruginosa is among the most dreaded Gram-negative pathogens in hospital setting and is the one of main causes of nosocomial infections [47]. According to the National Healthcare Safety Network (NHSN), P. aeruginosa was involved in 8% of HAIs in the US hospitals [48]. Moreover, in 2013, the CDC reported that about 51,000 health-care-associated P. aeruginosa infections occur in the US each year. More than 6,000 (13%) of these are multi-drug-resistant with roughly 400 deaths per year [49]. In the EU, P. aeruginosa represents 8.9% of total pathogens associated with nosocomial infections [45]. P. aeruginosa is an important cause of infection among patients with impaired immune systems. In 2012, high percentages of Multi-Drug Resistant (MDR) P. aeruginosa isolates were reported in several countries, especially in Southern and Eastern Europe. Combined resistance was common, with 14% of the isolates reported as resistant to at least three different antimicrobials [50]. Another bacterium causing similar problems is the Gram-positive S. aureus. Besides to being responsible for food poisoning outbreaks, this species has been recognized as an important pathogen which causes different serious human diseases [51]. S. aureus in its methicillin-resistant form (MRSA) is a major cause of anti-microbial resistant health-care associated infections worldwide. MRSA remains a public health priority in the EU, as the percentage of MRSA is still above 25% in seven of 29 reporting countries [52]. In the EU the number of patients acquiring health-care-associated infections in acute care hospitals has been estimated at 4.1 million each year [53]. S. aureus is the most involved pathogen in bloodstream infections in the US. According to the NHSN, this bacterium is associated with 15% of total HAIs reported between 2011 and 2012 in the US [54].

3. How bacteria adhere to surfaces and form biofilms?

Biofilm formation is a complex process which gives bacteria a better resistance to cleaning agents than bacteria growing under planktonic form [7]. Biofilm is a community of microorganisms in which cells stick to a surface and to each other (Figure 1).
Figure 1: Scanning electron microscopy image of biofilm produced by *Staphylococcus aureus* CIP 4.83 on 316L stainless steel after 24 h incubation at 37°C. The scale bars in the images are 2.5 μm (a) and 10 μm (b).

This cell cluster is marked by the secretion of extracellular matrix (Figure 2) with adhesive and protective properties [1,7].

Figure 2: Scanning electron microscopy image of *Escherichia coli* biofilm on Teflon. The arrows in the image point to the extracellular matrix enclosing the *Escherichia coli* biofilm bacteria (colored in pink). The scale bar in the image is 10 μm.

Biofilm formation requires different steps and there are a number of mechanisms by which many microbial species may come closely in contact with a surface, attach and promote cell-cell interactions in order to grow and form biofilms. Theses mechanisms have been widely described [55]. The different steps leading to biofilm formation are now well understood. The adsorption of bacteria or reversible adhesion to the surface is the first step of biofilm formation. It is triggered when the microorganisms approach the surface over 50 nm, through van der Waals interactions. Then, when the distance is between 10 and 20 nm, more non-covalent forces such as hydrophobic, acid-base and electrostatic interactions get involved in the adhesion process. As the distance decreases the adhesion becomes irreversible, and at less than 0.5 nm other specific interactions, also called short-range interactions, are needed to attach bacteria to abiotic surfaces (Figure 3). In fact, bacteria have some structural adhesins which are a part of the cellular envelope such as pili, Fimbria and flagella that enhance cellular adhesion. These structures create bridges between cells and surfaces and allow overcoming unfavorable conditions in order to strongly anchor bacteria to abiotic surfaces [56].

Once the irreversible adhesion is established, bacteria start synthesizing insoluble exopolysaccharides (EPS). Within hours of EPS accumulation, bacteria get entrapped in a complex protecting extracellular matrix and form a mature biofilm that provides protective environments against antibacterial agents and antibiotics [57]. Indeed, this EPS matrix makes traditional surface cleaning procedures and application of detergents or biocides on
materials in contact with food not fully efficient to eliminate mature biofilms [58]. Therefore, one of the most effective strategies to limit biofilm formation is to prevent or restrict bacterial adhesion on surfaces. Bacterial adhesion on abiotic surfaces and subsequent biofilm formation constitute a serious issue in several sectors such as food industries, water canalizations and medical facilities. Indeed, bacteria find favorable conditions to colonize surfaces and establish biofilms [7]. The persistence of biofilm in food, medical and other sectors constitutes reservoirs for pathogens which increase the occurrence of HAIs and FBDs. Thus, it is necessary to investigate different strategies in order to reduce the bacterial adhesion and the formation of biofilm.

Figure 3: The reversible bacterial adhesion consists in the initial attraction of the bacterial cells to the surface through the effects of non-specific physical forces (distance > 50 nm between bacterial cells and surfaces). The irreversible adhesion is achieved through the effects of the specific (short-range) interactions (distances < 5 nm, with involvement of hydrogen bonding, ionic and dipole interactions, hydrophobic interactions and bacterial structural adhesins).

4. Food-borne infections and adherent cells

Food contact surfaces and equipments are considered a serious factor contributing to contamination of foods if not properly cleaned [59]. In addition, surface contamination may lead to biofilm formation which enhances the capacity of food-borne bacteria to survive stress conditions encountered within food processing environments [60]. Surface contamination by pathogenic bacteria results in serious food-borne outbreaks generating a considerable disease burden and also economic losses [61]. The economic cost of food-borne outbreaks is highly affecting the US economy at a cost of 50 to 80 billion US dollar annually [62]. Other statistics has estimated that the total burden of FBDs was 152 billion US dollar [63]. In Australia and New Zealand, the cost of food-borne outbreaks has been estimated at 1,289 billion and 86 million US dollar respectively per year [64,65]. In Sweden, the annual cost of food-borne outbreaks was estimated to be 171 million US dollar [66]. In this regard, globalizing of food market with worldwide transportation makes food safety a major priority in order to prevent spreading of pathogenic bacteria and the emergence of food poisoning outbreaks worldwide. In England and Wales, FBDs cause more than 2 million cases, 21,138 hospitalizations and 718 deaths per year [67]. Pathogenic bacteria are able to adhere and form biofilms on various food contact surfaces [68,69]. It is now established that the persistence of pathogenic bacteria on food contact surfaces, equipment and processing environments, is a contributing factor in food-borne outbreaks, especially those involving L. monocytogenes, B. cereus, S. aureus, E. coli and Salmonella spp. [70]. Equipment, utensils and cutting boards are likely to be the key cross contamination routes as they become contaminated with pathogens from the handlers, sewage, water and condensation caused by the faulty ventilation [71–73]. Therefore, it has been reported that in the United Kingdom, 14 % of all food-borne illnesses involving S. aureus, E. coli, Salmonella enterica and L. monocytogenes, may be due to inadequately cleaned cutting boards and knives [74]. According to the French national health monitoring institute (InVS), 1,380 FBD outbreaks were reported in 2014, affecting 12,109 people, including 649 hospitalizations and 2 deaths. The three most frequently suspected pathogens were S. aureus (30%), B. cereus (22%) and Salmonella spp. (15%). The French available data showed also that food contact surfaces and equipment were up to 60 % involved in FBD outbreaks (2011) in collective and home catering [75]. In fact, food industries represent a favorable environment for bacterial adhesion and biofilm formation [76]. In the dairy, meat and sea-food industries food contact surfaces are often contaminated by pathogenic bacteria including L. monocytogenes, S. aureus, Salmonella spp., B. cereus and E. coli [77–80]. Moreover, it has been reported that even after cleaning, E. coli bacterial densities up to 10^5 CFU/cm^2 could be recovered on food processing surfaces [81]. It has been mentioned that in small-scale facility producing
traditional dry sausage, sixteen \textit{L. monocytogenes} strains and nine \textit{Salmonella} spp. subspecies were isolated from the stuffing machines [82]. Moreover, many pathogenic bacteria such as \textit{B. cereus} and \textit{S. aureus} are often isolated from the dairy, meat and sea-food industries surfaces [79]. In addition, a highest prevalence of \textit{sea} gene encoding for Staphylococcal Enterotoxin A (SEA) have been reported. The \textit{sea} gene is the most common in \textit{Staphylococcus}-related food poisoning [83].

5. Nosocomial infections and adherent cells
Nosocomial infections contracted during hospitalization can lead to high morbidity and even mortality of immune-depressed patients. Bacterial adhesion to medical devices surfaces and surgical sites is considered the base of the pathogenic mechanism [84]. Bacterial risk is of major concern in the medical sector because of the high rate of contamination of materials which are inserted into or in contact with the human body. Medical implants such as urinary catheters, central venous catheters and implanted prosthetic devices are prone to biofilm formation and represent a serious nosocomial infection source [85–87]. The issue starts when an indwelling medical device is contaminated with pathogenic bacteria which may develop a biofilm. Once these microorganisms irreversibly attach to devices introduced into a body, they start producing extracellular polysaccharides to develop an infectious biofilm. Such infections are known nowadays as chronic polymer-associated infection [88]. According to the National Nosocomial Infection Surveillance system of the CDC, Blood-Stream Infections (BSIs) represent 90% of all nosocomial blood infections and they are always considered to be device related if they happen after the insertion of an intravascular catheter [89]. Moreover, intravascular catheters are one of the most common causes of nosocomial bacteremia. In fact, catheter-related BSIs are affecting over 250,000 patients per year in US [90]. In this context, it has been shown by scanning and transmission electron microscopy that almost all indwelling catheters are colonized by microorganisms embedded in a biofilm matrix [91]. These biofilms may be located either on the lumen or on the outer surface of the catheter [92]. The colonizing microorganisms may originate either from patient’s skin micro-flora or other micro-flora from health-care staff and contaminated facilities. Furthermore, staphylococci are recognized as the most frequent causes of biofilm-associated infections [93]. The percentage of implant failure, due to infection by three different groups of staphylococci: MRSA, Methicillin-Sensitive \textit{S. aureus} (MSSA), and Coagulase-Negative Staphylococci (CoNS), is of ca 2% of all implants, representing an average of 4500 incidents per year [94]. Moreover, the prevalence of Ventilator-Associated Pneumonia (VAP) is 8 to 28% among patients who received prolonged mechanical ventilation [95]. This results from the respiratory system colonization by the endogenous flora or by exogenous pathogens acquired from the intensive care environment [96,97]. \textit{P. aeruginosa} is also considered one of the most frequently associated pathogen with HAIs. It has been identified that healthcare water systems are associated with patient infections with \textit{P. aeruginosa} in intensive care units [98]. In fact, \textit{P. aeruginosa} biofilms are likely to represent a potential reservoir source of nosocomial infection when it colonizes water systems in healthcare facilities [98]. Besides to their fatality towards human, HAIs represents a high economical cost. The annual direct medical cost of HAI to the US hospitals ranges from $28.4 to $33.8 billion [99]. In France the total cost of nosocomial infections in acute care units was estimated to be up to €3.2 million per year [100].

6. Parameters controlling biofilm formation
Abiotic surfaces are vulnerable to biofilm formation. Therefore, it seems to be necessary to understand the parameters that influence bacterial adhesion in order to find solutions against biofilm formation. Bacterial adhesion to surfaces is likely to be related to three main parameters which are the physiochemical characteristics of the bacterial cell and abiotic surfaces and finally the environmental conditions.

6.1. Role of the physiochemical characteristics of the bacterial cell surface in biofilm formation
The attachment of bacterial cells to abiotic surfaces is a process tightly related to several physiochemical forces such as van der Waals, electrostatic, steric forces and hydrophilic/hydrophobic. Moreover, the physicochemical surface properties of bacterial cells are determined by structures and molecules that are exposed on the cell surface which control the attachment and biofilm formation. Here, the major bacterial cell structures will be highlighted.

6.1.1. Role of bacterial cell surface structures
6.1.1.1. Flagella
Flagella have been generally considered major virulence factors mainly because of their motility property. However, flagella are getting recognized to play other roles with more functions besides motility and

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chemotaxis. Recent studies have defined flagella as an effective bacterial surface compound in many additional processes including adhesion, biofilm formation and virulence factor secretion [101]. Motility is considered a virulence factor facilitating the colonization of abiotic surfaces by pathogenic bacteria. According to different studies the flagellar motility is important for initial cell-to-surface contact leading to biofilm formation and development [102,103]. Flagella can facilitate the attachment of bacteria to surfaces by overcoming the repulsive forces that might hamper cell- to-surface contact. Thus, flagella are not only required for motility but also plays an important role in surface sensing and the earliest steps of surface adhesion that leads to the formation of a biofilm. E. coli and L. monocytogenes use flagella, pili, and membrane proteins to initiate attachment [104]. The loss of these cell appendages changes their surface properties which may lead to decreased attachment ability on some abiotic surfaces [105].

6.1.1.2. Fimbriae or pili

Fimbriae (or pili) are a group of rigid, straight, and filamentous proteinaceous structures composed of protein subunits called pilin associated to the outer bacterial membrane surface [106]. Their role in biofilm formation on abiotic surfaces is considered critical in the early stable cell-to-surface attachment. It has been showed that Type 1 and Type 3 fimbriae on Klebsiella pneumoniae strain surface are the main factors facilitating adherence and the formation of a full-grown biofilm on abiotic surfaces [107,108]. Moreover, fimbriae have a critical role in P. aeruginosa adhesion to SS, polystyrene and PolyVinyl Chloride (PVC) [109]. Type 1 fimbriae of E. coli facilitate attachment on abiotic surfaces and promote biofilm formation. In fact, it has been reported that the expression level of type 1 fimbriae had a direct effect on E. coli adhesion to surfaces [110]. Furthermore, it has been reported that the presence of type I pili is essential for the initial attachment of E. coli to PVC [111]. In fact, cells carrying lesions in genes encoding for the regulation or biogenesis of type I pili did not attach [111].

6.1.1.3. Extracellular polymeric substances (EPS)
The main composition of bacterial EPS includes polysaccharides, proteins, nucleic acids, lipids and phospholipids [112]. The lipopolysaccharide (LPS) outer layer of Gram-negative bacteria affects the bacterium’s susceptibility to disinfectants and influences the biofilm formation [113]. The pel genes encode proteins with similarity to components involved in P. aeruginosa’s polysaccharide biogenesis. The pel gene cluster is conserved in other Gram-negative bacteria and was previously identified in the P. aeruginosa PA14 strain as required for the production of a glucose-rich matrix material involved in the formation of a thick pellicle and resistant biofilm. Indeed, mutation in pel genes may lead to an adherence defect [114]. For E. coli, truncation of LPS affects the biosynthesis of Type 1 fimbriae and flagella resulting in a reduced adherence [115]. Alterations in the peptidoglycan structure exposed at the surface of L. monocytogenes can also have an effect on attachment [116]. Many bacteria produce EPSs which are an important constituent of the biofilm extracellular matrix. Overproduction of EPS can even inhibit initial attachment of E. coli O157:H7 to SS [117]. Several studies targeting the cell-surface proteins have revealed the existence of a large group of cell-surface protein called biofilm-associated proteins (Bap) on S. aureus. Recently, BapA was reported as necessary for biofilm formation by Salmonella Enteritidis [118]. Moreover, in Salmonella biofilms, cellulose is the main matrix EPS and represents the second component of EPS after the curli fimbriae. Cellulose is a β-1→4-D-glucose polymer which is biosynthesized by the bcsABZC-bcsEFG genes (bacterial cellulose synthesis) [119], two operons that are involved in cellulose biosynthesis in both Salmonella Enteritidis and Salmonella Typhimurium respectively [120,121]. Colanic acid, another EPS belonging to capsular extracellular polysaccharide, is essential for Salmonella Typhimurium biofilm. The importance of colanic acid in the biofilm formation capacity of Salmonella strains unable to produce either curli fimbriae or cellulose have also been confirmed [122].

6.1.2. Role of bacterial surface hydrophobicity in bacterial adhesion

In addition to the influence of the type of molecules expressed on the bacterial cell surface on the attachment to solid surfaces, there is a correlation between bacterial surface hydrophobicity and adhesion. In general, bacteria behave as hydrophobic particles. However, the degree of hydrophobicity depends on many parameters such as the pH, the ionic strength of growth medium and the bacterial species [123]. It has been reported that S. epidermidis strains with higher surface hydrophobicity adhered more than the ones with less surface hydrophobicity to polyethylene [124]. Hydrophobicity of bacteria can be evaluated by contact angle measurements, such as the sessile drop method or by their ability to adhere to hexadecane [125].

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6.1.3. Role of bacterial surface charge in bacterial adhesion

The surface charge of bacteria is another important physical factor for their adhesion [126]. Depending on their surface groups’ ionization, bacteria acquire a surface electric charge in aqueous suspension. In fact, bacteria have a net negative surface charge. The surface charge of bacteria varies according to bacterial species and is influenced by the growth medium, the pH and the ionic strength of the suspending buffer, bacterial age and bacterial surface structure [123]. The surface charge is usually characterized by the electrophoretic mobility (zeta potential) [125]. However, the contribution of bacterial surface charge to bacterial adhesion has not been clearly understood. The adhesiveness of *S. epidermidis* correlates directly with surface electro-negativity and hydrophobicity while the adhesion of *E. coli* is inversely proportional to the degree of negative surface charge but is not influenced by hydrophobicity [105].

6.1.4. Role of bacterial membrane potential in bacterial adhesion

Bacterial membrane potential is a physical characteristic that plays a dominant role in the adhesion of microorganisms to abiotic surfaces. Surface potential mapping using Kelvin probe force microscopy showed that the bacterial membrane potential is not the same on different material substrates [127]. The changes in bacterial membrane potential have been considered a direct result of changes in cellular metabolism and motility [127]. Adhesion has been shown to depend mainly on the pH, ionic strength of the suspending solution and of material surface properties. Some studies had also established that the membrane potential plays an important role in the bacterial adhesion on surfaces too [128].

6.2. Role of the physiochemical characteristics of the abiotic surface in biofilm formation

The main factors influencing bacteria adherence to abiotic surfaces include the physiochemical properties such as surface energy and hydrophobicity, chemical composition of the solid surface and surface roughness [126].

6.2.1. Chemical composition of the solid surface

Bacterial adhesion to surface and biofilm formation depend on the solid surface chemistry. Surfaces can have different functional groups that influence the bacterial attachment which depends also on the hydrophobicity and charge of material [123]. *S. aureus* was found to adhere preferentially to metals and *S. epidermidis* to polymers [129]. This result may explain why *S. epidermidis* often causes polymer implant infection while *S. aureus* is often the major pathogen in metal implant infections. The surface chemistry might be modified with different types of coating. The most current is plasma coatings that considerably reduce bacterial adhesion to surfaces [130]. Different studies have shown that the hydrophilicity of the native PVC was altered after thiocyanation of PVC surface, resulting in the decrease of bacterial adhesion to this material [131]. It has been reported that nisin-coated surfaces also inhibited the bacterial adhesion [132].

6.2.2. Surface topography and roughness

The relationship between bacterial adhesion and the surface topography was studied intermittently for 45 years [133]. Thus different opinions on the effect of the surface roughness on bacterial adhesion and biofilm formation have emerged. The food hygienic quality is closely related to the cleanability degree of equipment used in the production lines. The roughness of SS is considered a primary factor in the attachment of bacteria and biofilm formation [134]. The influence of material roughness on the bacterial adhesion has been investigated closely. Many studies focusing on the topography of different types of surfaces have found that the irregularities of abiotic surfaces enhance bacterial adhesion and biofilm formation whereas the smooth surfaces decrease the ability of bacterial adhesion [135]. In fact, rough surfaces have a greater surface area and provide for bacteria protective shelter against cleaning agents and more favorable sites for colonization (Figure 4) [76]. Moreover, porosity of materials has a significant effect on the bacterial attachment. It has been found that implant site infection rates are different between porous and dense materials with porous materials having a much higher rate. This shows that bacteria adhere and colonize the porous surface preferentially. Indeed, bacteria adhere more to porous and grooved surfaces compared to dense and flat ones because of their larger contact surface [135].

6.2.3. Surface energy and hydrophobicity degree

The physiochemical properties of abiotic surfaces in food processing industry are suspected to significantly influence the biofilm formation mainly via the initial attachment of bacteria. In fact, the attachment of the bacteria depends on the critical surface tension of the solid surface [136].
The surface energy of a solid surface is a direct indicator for interfacial attractive forces. The modification of the surface energy of surfaces has a direct influence on the bacterial adhesion [137]. It has been reported that the adhesion of S. xylosus depends on the physicochemical properties of the surface and ionic strength of the surrounding medium [138]. It has been defined that hydrophobic interactions are the strongest of all non-covalent interactions in biological systems [139]. Physicochemical forces involved in adhesion are dependent of each other. The relationships between surface hydrophobicity and charge have been observed. A decrease in surface charge is often accompanied by an increase in hydrophobicity [56]. Surface hydrophobicity has been considered a determinant factor for microbial cell adhesion [140]. The concept of hydrophobicity opposes that of surface wettability since hydrophobic surfaces present low wetting. Furthermore, hydrophilic surfaces generally allow greater bacterial attachment and biofilm formation than hydrophobic ones [141]. It has been defined that initial attachment of L. monocytogenes Scott A to SS was more rapid than to rubber [142]. Moreover, several studies have investigated the relation between the hydrophobicity degree and the bacterial adhesion rate. The relationship between the hydrophobicity degree of different abiotic surfaces and the number of attached S. epidermidis and Alcaligenes denitrificans cells have been assessed and results showed that the adhesion rates increased with the surface hydrophobicity [143]. In the same context, Sheng et al. (2008) [144] have reported that bacterial adhesion is lower on metal surfaces with reduced hydrophobicity.

6.3. Environmental conditions influencing bacterial adhesion

The physicochemical properties of both cell and material surfaces are very critical proprieties affecting the adhesion of bacteria and the formation of biofilm [145]. Moreover, bacterial adhesion is an extremely complicated process that is affected by many other factors including the environmental conditions (pH, temperature, bacterial concentration, nutrient availability and the associated flow conditions) that need to be controlled in order to find strategies against biofilm formation [68]. The number of attached bacteria is significantly affected by the flow conditions and generally the number of attached bacteria decreases when shears rates are high. Moreover, variations in pH value in the culture environment also influence bacterial adhesion and the growth of biofilm [146]. The pH influences the cell surface hydrophobicity and better adhesion to hydrophobic surfaces was found at pH in the range of the isoelectric point when bacteria are uncharged [147]. Therefore, pH influences bacterial adhesion by influencing the surface charge and changing surface characteristics of the bacteria [55]. Moreover, variations in external pH can disturb the trans-membrane electrochemical gradient and have a biocidal effect on the microorganisms. The growth temperature is also an important condition for bacterial adhesion and biofilm formation as well as the presence of nutrient [1,148]. High growth temperature was found to increase the biomass and the attachment ability of bacteria probably, due to the production of heat stress proteins associated with the cell surface [149,150]. Otherwise, different studies concerning S. aureus biofilm formation have shown that temperature variation has no clear effect on the biomass [151]. Thus, optimum temperature enhances the biofilm formation. Temperature also affects the bacterial surface polymer composition which decreases at low temperature and reduces the adhesive properties of bacteria [152]. Another important factor in biofilm formation is nutrient availability. In fact, nutrients influence the surface charge of bacteria. For instance, glucose and lactic acid in the growth medium decreased.
the bacterial cell wall electro-negativity through the neutralization of the surface charge [153]. Thus, a synergistic effect between the environmental factors may occur and affect biofilm formation.

7. Strategies to control biofilm formation and development

Virulence of microorganisms is often enhanced when imbedded into biofilm [154]. Unfortunately, in the industrial fields, the availability of nutrient and water promotes the biofilm formation. In this regard, several strategies have been proposed to control biofilm formation and to avoid biofouling. Ideally, preventing biofilm formation would be a more logical option than treating it once established. Thus two major ways to control biofilm formation can be adopted. The first one is based on the use of antimicrobial agents, physical forces, enzymes, plant extracts, etc. to eradicate or disrupt already formed biofilms. The second strategy aims to anticipate and prevent bacterial adhesion and therefore biofilm formation by modifying the physiochemical properties of abiotic surfaces.

7.1. Eradication of biofilms

7.1.1. Cleaning and disinfecting of abiotic surfaces

In food processing industry, effective cleaning and disinfecting of equipment and surfaces is required to reduce the bacterial contamination and produce safe products with acceptable shelf life and quality [155]. Cleaning is the first step of sanitizing intended to reduce the number of pathogenic bacteria on surfaces before disinfecting [155]. An efficient cleaning and disinfection procedure consists of a sequence of rinses using good quality water with application of detergents and disinfectants [155]. Cleaning frequency must be clearly defined for each process line (daily, after production runs, or more often, if necessary). Cleaning is an important step to minimize microbial colonization of industrial food processing equipment. It seems to be of great importance to eliminate as many micro-organisms as possible before applying a disinfectant [156]. In food and health sectors, disinfectants are used for decontamination and to reduce the surface population of viable cells left after cleaning in order to prevent microbial growth and biofilm formation on surfaces [112]. There are different kinds of commercialized disinfectants such as alcohol based one, hypochloric solutions, aldehydes, hydrogen peroxide, ozone and quaternary ammonium compounds (QACs) [1]. These disinfectants can be used in different sectors at different concentrations [157]. The particularity of these antimicrobial agents is that they have more than one target site. In fact, they can target the cytoplasmic constituents, the outer cell components and the cell cytoplasmic membrane [158]. The activity and the efficiency of disinfectants against biofilms depend on several chemical and physical factors such as concentration, pH, temperature and contact duration. Moreover, the surface type may also affect the efficacy of biocides against biofilms [1]. The involvement of surface type is mostly related to the nanoscale surface morphology which affects the biofilm architecture and weakens the effectiveness of cleaning and sanitizing procedures [159].

7.1.1.1. The biofilm resistance to disinfectants

Micro-organisms are generally adhered to surfaces under a biofilm state. Disinfectants are often used at very high concentrations relative to their minimal inhibitory concentrations in order to make it impossible for bacteria to overcome the massive damage and develop resistance [160]. Many studies have shown that bacteria exposed to disinfectant levels lower than those required to deliver a lethal insult might develop resistance. In fact, the cells living under a biofilm state can be up to 1000 fold more resistant to disinfectant agents than their planktonic counterparts [1]. Thus, the disinfectant agents are frequently inefficient in the eradication of biofilms and increase the risk of severe health problems and economic losses. In fact, there are many strategies evolved by biofilm cells to achieve or increase their resistance: (1) Diffusion limitations of disinfectants in biofilms, (2) The phenotypic adaptations of biofilm cells to sub-lethal concentrations of disinfectants and (3) presence of disinfectant-adapted and persister cells.

7.1.1.1. Diffusion limitations of disinfectants in biofilms

A mature biofilm is characterized by the production of an extracellular matrix composed of exopolysaccharides (EPS), proteins and lipids [161,162]. The multiple layers of cells and EPS may constitute a complex and compact structure which prevents disinfectants from penetrating and reaching the internal layers, thus hampering their efficacy. It has been shown, that the disinfectant’s diffusion and reaction limitations are involved in the biofilm resistance [163]. In fact, several studies have found that the restricted diffusion of disinfectant molecules was related either to the size exclusion or the electrostatic interactions. The interactions between antimicrobials and biofilm components seem more likely to explain the limitations of penetration into
the biofilm [164]. Moreover, the electrostatic interactions of the biofilm matrix seem to have an important role in the resistance to biocides [165].

7.1.1.1.2. The phenotypic adaptations of biofilm cells
Different studies have illustrated the role of extracellular matrix in the resistance of biofilms. Nevertheless, other investigations have shown that despite an effective penetration of disinfectants into biofilm, only a low level of resistance was achieved [166]. Thus, other mechanisms based on the phenotypic adaptation such as reduced growth rate and metabolism [167,168], membrane permeability/fluidity [169], phenotypic adaptation and gene expression [170,171], could be involved in the resistance of biofilms to biocide agents.

7.1.1.1.3. Presence of disinfectant-adapted and persister cells
Food and medical environments constitute a reservoir of bacteria which have developed tolerance to disinfectants misused at lower concentrations than that recommended by the manufacturer [172]. Moreover, bacteria may develop cross-resistance to different disinfectants [173]. The involvement of a subpopulation of persister cells in the biofilm may account for the observed resistance to biocides. Persisters are highly tolerant to disinfectants and may have adapted a highly protected, perhaps spore-like, state [174].

7.1.2. Treatment with plant extracts
The use of bio-based antimicrobial agents can be an effective alternative for the control of biofilm formation. One approach may be the use of plant essential oils (EO) which have been used since many centuries to fight against different pathogens including bacteria, fungi and viruses [175]. The cumin seed EO was found to reduce the K. pneumonia biofilm formation. Fadli et al. (2012) [176] have demonstrated the synergistic effect of ciprofloxacin and EO of endemic Moroccan thyme species, on antibiotic-resistant bacteria involved in nosocomial infections. Essential oils may damage the cell wall and membrane, leading to cell lysis and leakage of cell contents [177]. In addition to their high ability to kill bacteria, essential oils do not promote the acquisition of resistance unlike antibiotic and chemical disinfectant [178]. It has been shown that selected antimicrobial essential oils can eradicate bacteria within biofilms with higher efficiency than certain important antibiotics, making them interesting candidates for the treatment of biofilms [179]. Moreover, other plant extracts seem to have highly effective anti-biofilm activity [180] and represent promising strategies to overcome resistant biofilm formation.

7.1.3. Mechanical and enzymatic treatments
Chemical based agents used for disinfection possess several disadvantages such as their toxicity, generation of chemical wastes, reaction with materials and promotion of the bacterial resistance. In order to overcome these disadvantages, new approaches including applying mechanical forces and enzyme have been proposed. Mechanical cleaning of surfaces is probably the simplest and most successful way to remove biofilms and maintain surfaces clean [7,181]. The newer physical methods used for the control of biofilms include super-high magnetic fields [182] and ultrasound treatment [183]. Enzymes can be used to effectively eradicate biofilms in the food industry. Several studies have demonstrated that DNase1 reduced biofilm biomass by approximately 40% among all tested Gram-positive (S. aureus and Streptococcus pyogenes) and Gram-negative bacteria (Acinetobacter baumannii, Haemophilus influenza, K. pneumoniae, E. coli, and P. aeruginosa) [184,185]. Lysostaphin (LS) is a naturally occurring enzyme that can effectively penetrate into biofilms [186]. The LS was found to be capable of eradicating biofilms of all S. aureus and S. epidermidis strains [187]. Different enzymes, such as, protease, α-amylase, b-glucanase, and endoglucosidase have been reported to be effective in the removal of biofilm of different pathogens [182]. Nevertheless, a combination of different enzymes and antimicrobials/disinfectants is a promising, highly effective method for removing and controlling biofilms.

7.1.4. Bacteriophage treatments
Bacteriophages treatment is a nowadays major strategy of the biofilm control and removal. Bacteriophages are naturally occurring viruses that infect bacteria within biofilms [188]. Phages have been used for the treatment of human infectious diseases [189]. The use of phages to control biofilms has potential for several reasons. Phages can replicate at the site of an infection. During the lytic replication cycle, the infection of a bacterial host cell by a single phage virion will result in the production of other progeny phage, depending on the particular phage and host strains. Some engineered enzymatic bacteriophage produce enzymes that degrade the biofilm EPS matrix which represents promising tool of biofilm control [190]. Moreover, biofilm removal by enzymatic bacteriophage has been found to be more efficient than the classical enzymatic treatment [191]. It has been reported that a combined use of the bacteriophage K and a novel DRA88 bacteriophage has showed successful
effect in reducing the *S. aureus* biofilm formation [192]. The phage mixture may form the basis of an effective treatment for infections caused by *S. aureus* biofilms. Similarly, lytic bacteriophages were found to be efficient in the prevention and eradication of biofilms of different pathogenic bacteria [193].

7.1. Prevention of biofilm formation by the modification of abiotic surfaces properties

In food industry, all surfaces are subjected to bacterial contaminations since exposed to air, humidity or diverse environmental conditions. To overcome these problems, several strategies involving the modification of surface physicochemical properties have been used in order to set up antimicrobial surfaces which reduce bacterial adhesion and prevent biofilm formation.

7.1.1. Bactericidal/Bacteriostatic coating

Modifying the surface properties of food contact surface or indwelling medical devices is one of the main focuses to prevent or decrease bacterial colonization and biofilm related infections. Coating the material surface with bactericidal/bacteriostatic substances seems to be an innovative approach to make surfaces resistant to bacterial adhesion and biofilm formation. It has been shown that *S. epidermidis* biofilm formation was significantly inhibited on titanium implant surfaces coated covalently with vancomycin [194]. However, the use of antibiotics can lead to antibiotic resistance and even induce biofilm formation [195]. The effectiveness of a nisin coating onto Low density polyethylene in reducing the population of *L. innocua, L. monocytogenes, B. cereus* and *S. aureus* has been demonstrated in a recent study [132]. Moreover, implant surfaces such as titanium have acquired antibacterial properties after being coated with hydroxyapatite [196]. Silver particles, well-known as one of the strongest bactericidal agents, were also used as an anti-biofilm coating on polymer and metal surfaces [197]. It has been demonstrated that biofilm formation by a number of pathogens on silver nanoparticle coated catheters was almost completely prevented [198]. It has been reported, also, that silver-based coatings are widely used in medical implants due to the bactericidal effect of the released silver ions from the surface, against both Gram-positive and Gram-negative bacteria [199,200]. Surfaces possessing chemically bonded hydrophobic QACs have shown bactericidal properties [201]. Glass surfaces were coated with QACs functionalized silica nanoparticles and exhibited inhibition of growth and accumulation of Gram-negative and Gram-positive bacteria [202]. QACs coated surfaces have been shown to damage bacteria by the disruption of their cellular membranes [201]. The perturbation in the lipid bilayers occurs when the positively charged nitrogen in the ammonium group interacts with the negatively charged groups of acidic phospholipids in the bacterial cellular membrane [203]. This causes the perturbation of low-molecular-mass solutes efflux. In fact, under the action of QACs, bacterial cells release their potassium ion, which in turn causes the cell to lose its ability to undergo osmo-regulation and other physiological functions, resulting in the cell death [204]. Unlike silver ions which have a release-based antibacterial mechanism [205], QACs coatings possess a long-lasting contact-based antibacterial mechanism [206]. Despite these properties, it has been reported that bacteria are able to develop resistance against these modified surfaces [207]. To improve the antibacterial effect of coated surfaces, many studies have investigated combinatorial approaches of different antibacterial molecules. The combined release of silver and the contact-killing abilities of QACs have shown a synergistic antibacterial effect [208]. Nitric oxide loaded nanoparticles have also been reported to be bactericidal [209]. It has been suggested that the antibacterial effect of nanoparticles arises from their physicochemical properties. In fact, due to their nano-metric size, these particles are capable to carry the antimicrobial molecules and accumulate near the cytoplasm, which kills the cells. Moreover, some of these nanoparticles might possess oxidizing power by generating reactive oxygen species [210,211].

7.1.2. Immobilization of bioactive compounds.

Bioactive molecules can be attached onto polymers in two different ways. The choice of the antimicrobial agent immobilization technique depends on the expected behavior of the modified surface. Indeed, for setting up active antimicrobial surfaces, the immobilization may be done either chemically in a covalent manner or physically by a simple adsorption [15]. In case of chemical immobilization, the antimicrobial agent is strongly fixed onto the surface providing a long term action and does not migrate from material surface to the food such as modified polymers used in food transformation platforms. When the bioactive molecules are immobilized by adsorption the antimicrobial effect is achieved with migration. Thus, such antimicrobial surfaces may be intended for biomedical applications and not only for food sector [15].

Non-covalent adsorption is mainly governed by hydrogen bonding, van der Waals forces, electrostatic and hydrophobic interactions between the antimicrobials and the polymer surfaces [15]. Non-covalent methods provide short-term applications because antimicrobials are released from the polymer. The factors affecting
bioactive molecules adsorption on surfaces depend on the surface physiochemical properties, the characteristics of the bioactive molecule itself and the environmental factors [15]. However, covalent immobilization provides the most stable linkage between the antimicrobial molecule and the functionalized polymer surface that usually requires the use of cross-linkers or “spacer” molecules that link the functionalized polymer surface to the bioactive agent [15]. In fact, covalent binding may alter the conformational structure and the active site of the bioactive molecules such as enzymes and thus, may affect their activity. This lack of activity can disturb the effectiveness of the modified surfaces. Thus, the parameters affecting the antimicrobial performance of immobilized bioactive agents (concentration of bound antimicrobials, spacer choice, length and flexibility) need to be controlled. Spacers or cross-linkers are hydrophilic molecules used for attaching bioactive compounds, such as, enzymes which may lose activity when linked directly to a solid surface because of steric constraints. For example, Poly Ethylene Glycol (PEG) is often used to cross-link enzymes to substrates. Indeed, PEG may shield the enzymes from denaturation and maintains their bioactivity by keeping their active site in the appropriate conformation [212]. PEG was used to tether trypsin and lysozyme onto SS in order to prevent biofilms formation [213]. In another study, the anticoagulation properties of immobilized heparin were improved by using a PEG spacer when compared to heparin immobilized directly to the polymer surface. Using PEG seems to be an interesting process to increases the bio-specificity of tethered bioactive compounds [214]. Furthermore, using poly-functional reagent allows increasing the number of reactive sites available on a surface for immobilization of bioactive compounds [214]. The major drawback in utilizing a highly poly-functional agent tether is overcrowding of the functional groups which may reduce the immobilization of bioactive compounds, or that bioactive compounds are sterically hindered [214].

7.1.2. Initial surface modification and anti-biofouling effect of antibacterial surfaces

The anti-biofouling surface could also be achieved by depositing a thin layer of anti-adhesion coating on the surface to reduce attachment of pathogenic bacteria. The physicochemical properties of the surface have a direct effect on the ability of microorganisms to adhere to abiotic surfaces. Thus, it is believed that the surface chemistry and/or surface architecture and topography of the surface control their anti-biofouling behavior [215–217]. The sub-nanometre and nanometre roughness scales of metallic surface have shown differential anti-biofouling properties against bacteria. It has been reported that P. aeruginosa cells are unable to trigger their attachment on such surfaces. Recently, it has been shown that slippery liquid-infused porous surfaces prevented 99.6% of P. aeruginosa, 97.2% of S. aureus, and 96% of E. coli biofilm attachment over a seven days period under both static and physiologically realistic flow conditions [218]. Surface properties of materials or medical devices including chemical composition and reactivity, hydrophilicity/hydrophobicity [219], roughness [220] and charge can be modified by introducing a variety of coating, or surface modification to setup the desired anti-biofouling characteristics without altering the bulk properties of materials. The surfaces of SS and titanium have been coated using TriMethylSilane (TMS) plasma nano-coatings based on low temperature plasma technology [130]. These TMS plasma coated materials have significantly reduced the S. epidermidis adhesion and biofilm formation. In fact, the decreased bacterial adhesion to the coated surfaces can be associated to the decreasing protein adsorption after surface properties modification. Anti-biofouling coatings prevent biofilm formation at early stages which should be more desirable in food and medical settings. However, it is necessary to understand the mechanism by which adhesion is hindered to improve the efficiency of the coatings. Moreover, different techniques can be used to modify the surface properties, depending on the material application.

8. Applications

The different processes and techniques discussed above have been investigated with the goal of developing specific applications of bound bioactive molecules to surfaces within a wide range of scientific disciplines. Several applications in different sectors are cited below.

8.1. Food industry and other field application

In food processing industry, antimicrobial polymers such as active packaging can be used to improve food safety [221]. Immobilized lysozyme, glucose oxidase, and chitosan have been applied to set up antimicrobial packaging films. These packaging technologies could play a role in extending shelf-life of foods and reduce the risk of growth of pathogenic microorganisms by direct contact of the package with the food product [222]. Several compounds have been proposed and tested for antimicrobial activity in food packaging including organic acids, antibacterial peptides and fungicides [132,223–225]. In addition, antimicrobial food-contact surfaces include cutting boards and dishcloths which contain triclosan are found to reduce effectively the bacterial contamination [225]. It is important to optimize, rather than simply maximize, the density of the surface immobilized bioactive compound. In the case of enzyme immobilization, too many surface functional
groups can lead to overcrowding attachment of the enzyme, which result in reduced overall bioactivity after denaturation [226]. Moreover, it is necessary to exercise responsibility in using bioactive compounds in order to set up antibacterial surfaces. Indeed, several studies have shown the impact of antimicrobial agents in promoting development of resistant strains [227,228]. When surface modification strategies are applied to obtain antibacterial food processing surfaces, they can help reduce biofouling and cross-contamination. Fouling of process equipment in the dairy industry is one of the main issues to be solved. Despite, the corrosion resistance of SS, still today, when exposed to chloride solutions, localized corrosion can appear [229]. Many strategies have been taken in consideration to bend the corrosion of metallic material [230]. The effectiveness of coating SS with anticorrosion undercoat paint was investigated in several studies [231].

8.2. Biomedical application
Modified abiotic surfaces expected to be used inside or in contact with human body have to meet the demands required for both their surface and bulk properties. For the medical purpose, modified materials are not recommended if the substance will leach out causing cytotoxicity [232]. Metal ions release from metallic materials implanted into human body may cause various health problems such as metal accumulation in organs, allergy, and carcinoma [233–235]. The most important property that a modified abiotic surface must involve is biocompatibility. The biocompatibility of antibacterial QACs that are commonly used as disinfectants in hand solutions, cosmetics, and environmental treatment plants have been recently reviewed [236]. Biocompatibility can be divided into two kinds. One concerns the bulk property of the biomaterial, the other its surface property. The bulk biocompatibility is critical for the implantation of biomaterials. In fact, the rigidity of modified implants must match with that of the adjacent tissue, otherwise, hyperplasia or absorption of the tissue will prevail, resulting in failure of implantation. The second kind includes interfacial biocompatibility between the biomaterial and the living adjacent tissue which may induce rejection reactions towards the foreign-body. Biomaterial surface can be modified to influence the interactions between the material and the biological environments. For example, general biocompatibility can be imparted by immobilizing a hydrophilic polymer such as PEG to reduce protein adhesion since the pathway leading to blood coagulation begins with surface protein adhesion [237]. Several studies have mentioned different applications of a variety of modified biomedical devices [238,239].

9. Appropriate controls
When polymer surfaces are modified or grafted with bioactive compound, it is important to include appropriate controls. Surface functionalization is a multi-step process during which surface properties are often modified. It is not only important to compare bioactivity of the modified polymer, but also to evaluate bioactivity of the surface modified polymer to which the bioactive compound has not yet been attached. By this control, one can identify whether the change in bioactivity is due to the presence of the bioactive compound or simply a change in polymer surface chemistry. In some applications, the bond between the bioactive compound and the polymer surface must be covalent. Alternatively, in applications where a covalent linkage is necessary, comparing the quantity of biomolecule bound to unmodified polymer surface, functionalized polymer surface with or without the use of cross-linker may add value to the drawn conclusions as well as the potential commercial applicability.

The design of materials intended to be in contact with food must comply with rules of food compatibility. Food-contact materials are intended to come in contact with food. Thus, there is the possibility of the chemical substances migrating from the material to the food, which could be potentially harmful to human health [240]. Indeed, regulation must involve the antimicrobial substances in food packaging or modified food transforming devices, since, they are considered food additives if they migrate to food [241]. In response to this issue, many countries have implemented food contact regulations to ensure food safety [242,243]. Therefore, packagings and materials intended to come into direct contact with food are highly regulated around the world and must comply with several requirements that have been laid down at the European level. Within that context, regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food was published on the 14th of January 2011 [244]. In the US, antimicrobials in food packaging that may migrate to food are considered food additives and must meet the food additive standards. Packaging forms include bulk food storage containers, paperboard cartons, plastic or paper food wraps, jars and bottles [222]. Examples of antimicrobial uses include surface sanitizing solutions for milk containers, hydrogen peroxide uses in aseptic packaging, and antimicrobials impregnated into food packaging to protect either the package, or to extend the shelf-life of the food. It is possible that compounds that are not approved food additives could be transformed into approved additives during the migratory process. In food processing industries, it is also of great importance that these materials be easy to clean in order to limit their contamination with pathogenic bacteria. In
fact, in food industries, particularly the open working surfaces, the environment is propitious for contamination by microorganisms. Thus, the choice of materials excepted to be in contact with food is crucial. These materials have to withstand the potentially harsh environmental conditions such as high pressure, high concentrations of alkalis and acids, high temperatures, while remaining cleanable. Moreover, these materials must have qualities such as: corrosion resistance, non-toxicity, mechanical stability. Further considerations must concern the cost of such process to set up antimicrobial surfaces which may be susceptible to be expensive. Thus, this may have impact on their commercialization. The approval of surface modified medical devices by regulatory agencies like the International Organization for Standardization (ISO) requires that biocompatibility assessment be conducted to assure safety of the device or material. The primary guidance for the US, EU and Japan and associated countries has formally become the ISO 10993 standards, with each having reference to their own regulations only in special cases. The concern with devices and biomaterials is what migrates from the material into the body. It should be noted that there is ISO guidance (ISO 10993) for medical device risk assessment by the identification and quantification of chemical substances that can be extracted from a device over a period of time after the device would be prolonged (or introduced) into internal patient contact. The potential biological risks to patients must be assessed and allowable limits of exposure established. Thus, modified medical material must comply with the tests mentioned in ISO 10993 standards [245]. ISO 10993 concerns the following points, under the general title: biological evaluation of medical devices [245]:

- Tests for cytotoxicity, genotoxicity, sensitization, carcinogenicity and reproductive toxicity
- Tests for interactions with blood
- Tests for local effects after implantation
- Identification and quantification of potential degradation of medical material (polymers, ceramics, metals and alloys
- Toxicokinetic study design for degradation products and leachables in order to establish allowable limits for leachable substances

Conclusion

Biofilm formation is one of the main concerns that demand to elaborate effective strategies for their prevention or eradication in the food and medical sectors. In both sectors, several factors may enhance the bacterial colonization and biofilm formation on food contact surfaces and medical devices. Therefore, it is of great importance to understand the mechanisms of bacterial adhesion to these surfaces in order to reduce the surface contamination. Furthermore, biofilm is an adaptive form of bacterial cells to hostile environments which allow developing high resistance to disinfection treatments. Thus, it is of interest to understand the relationship between the environmental conditions of biofilm formation such as temperature, surface type, and biofilm age, and the biofilm resistance, in order to control the issues related to biofilms and improve the anti-biofilm treatments.

Furthermore, antibacterial surface development is nowadays an expending research field. This review gives an overview of the current approaches that aim to design antibacterial surfaces for food and medical applications. Antibacterial surfaces are expected to provide two distinct performances. Either they are capable of repelling bacterial cells, preventing their attachment and the initialization of biofilm formation or they inactivate/kill cells that do come into contact with them. Several antibacterial agents have been used to obtain antibacterial surfaces. Therefore, their mechanisms of action must be understood beforehand. Moreover, the durability, specificity and the procedure of the modification needs to be thoroughly evaluated in order to minimize costs. Since, these bactericidal mechanisms rely on the surface structure modification, they may help reduce the chemical wastes generated by the traditional, chemical-based approaches.

In the same context, as the old adage goes “an ounce of prevention is worth a pound of cure”, it is wiser to act at the source of the problem by hindering bacterial adhesion to abiotic surfaces instead of lately fighting already established biofilm. In fact, more consideration should be given to the design of anti-biofouling surfaces by focusing on the impact of the surface topography, charge and hydrophobicity on the initial adhesion of bacteria. Biocompatibility is an important point to take into consideration when we deal with materials that are susceptible to be in direct contact with human body or food. Thus, it is necessary to investigate the toxicological effect of the antibacterial surface employed in both health and food sectors.

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