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Biobased Polymers

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Under the editorship of Patrick Navard and a panel of experts, the series will include contributions from many of the world's most authoritative biobased polymer scientists and professionals. Readers will gain an understanding of how given biobased polymers are made and what they can be used for. They will also be able to widen their knowledge and find new opportunities due to the multidisciplinary contributions.

This series is aimed at advanced undergraduates, academic and industrial researchers and professionals studying or using biobased polymers. Each brief will bear a general introduction enabling any reader to understand its topic.

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Bioactive Functionalisation of Silicones with Polysaccharides

Springer

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Abbreviations

AAL	Allylalcohol
AAM	Allylamine
AFM	Atomic force microscopy
ALGA	Alginic acid
ASM	Active surface modification
BSA	Bovine serum albumin
CAC	Critical association constant
CAUTI	Catheter-associated urinary tract infection
CFU	Colony-forming units
Chi/CT	Chitosan
CLSM	Confocal laser scanning microscopy
CMC	Critical micelle concentration
CMChi/CMCT	Carboxymethyl chitosan
CVC	Cardiovascular catheter
FDA	Food and drug administration
FTIR	Fourier-transform infrared
GMK	Green monkey kidney
HA	Hyaluronic acid
HEMA	2-hydroxiethylmethacrylate
HSA	Human serum albumin
LCC	Local carriers or coatings
LDH	Lactate dehydrogenase activity
MIC	Minimum inhibitory concentration
MKM	Lysine-derived cationic surfactant
MTT	(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay)
PBS	Phosphate buffer saline
PDMS	Polydimethyl siloxane
PEG	Polyethylene glycol
PEMA	Poly(ethylene-alt-maleic anhydride)

PET	Polyethylene terephthalate
PSM	Passive surface modification
PTFE	Polytetrafluoroethylene
PVC	Polyvinyl chloride
QCM-D	Quartz crystal microbalance with dissipation
RH	Relative air humidity
SEM	Scanning electron microscopy
TOS	Tosufloxacin
USA	United States of America
UTI	Urinary tract infection
UV	Ultraviolet
UVO	Ultraviolet ozone
XPS	X-ray photoelectron microscopy

Introduction

This book deals with the surface functionalisation of silicones, used as medical implants. Its main focus is on urethral catheters as medical implants. Surface functionalisation of urethral catheters has some specifics but also some general approaches; therefore, the described modifications can be transferred to other medical implants made of silicone as well.

The development of antimicrobial and antifouling surfaces for materials used as urethral catheters has been in the interest of the medical community for several decades as urinary tract infections (UTIs) have shown to be amongst the most prevalent ones having the highest occurrence of all infections in health institutions. Statistical data indicates that amongst newly submitted patients, 23% of all infections are UTI. 80% of which are catheter-associated UTI (CAUTI) [1]. Urethral catheters are being used by 5–10% of patients in long-term care, mostly incontinent males and females [2]. Incontinence is a major reason for catheterisation since it affects 50% of the elderly population and 25% of these receives catheter treatment during hospitalisation [1]. In the USA, 40% of all infections patients get during hospitalisation are UTI with a mortality rate of 3% [3]. It has been shown that the major reasons for the appearance of CAUTI are errors in catheter management, such as opening a closed drainage system or false handling during insertion and usage of the catheter [4]. The European program of CAUTI prevention, therefore, includes (i) education of the staff regarding the indication of dates of catheter insertion and removal, (ii) documentation of catheter insertion and use, (iii) the selection of appropriate catheter materials and (iv) its catheter maintenance [5].

Besides the health issues, curing CAUTI also has a considerable economic impact. The overall cost for medical treatment of UTI in USA is staggering, with around 450 million US$ spent annually to manage these infections. The cost for treatment of one episode of CAUTI is approximately 2900 US$ [6, 7]. The European Union is facing the same problems, from all the patients suffering from UTI, 63% are CAUTI, with a mortality rate of 1.8%. Most of which are elderly

people. This problem will be even more pronounced in the future due to the fact that by 2050, it is projected that the global population aged 65 years and above will triple.

The presence of an indwelling urethral catheter bypasses the normal defence mechanisms of the host and allows microorganisms' continuous access to the urinary bladder. The microorganisms can ascend on the inner or outer surface of the catheter and persist once they reach the bladder [2, 3]. The presence of pathogen bacteria in the urine is referred to as bacteriuria and can lead to life-threatening illnesses and even death [4]. The number of viable bacteria in the urine during bacteriuria is over 105 CFU/mL [3]. The majority are faecal contaminants or skin residents from the patient's own microflora that colonise the periurethral area [6]. In 3–7% of the patients, new UTI causing microorganisms to appear in the urine daily. With such a trend, the prevalence reaches 100% in 30 days of catheter use. The prevalence is a statistical quantity used in the field of epidemiology describing the disease frequency of a statistical population in a certain time period. The use of an indwelling urethral catheter increases the prevalence for UTI for thirty times when compared to UTI prevalence for patients without urethral catheter [2]. The normal defence mechanism of the human host when bacteria bind to the bladder mucosa is inflammation that results in an influx of neutrophils and sloughing of epithelial cells. Both processes contribute to clearance of the bacteria from the mucosal surface. The urethral catheter does not possess such inherent defence mechanisms and bacteria can easily colonise its surface leading to the formation of a biofilm which causes additional problems in the process of preventing and curing of CAUTI [8].

The first step in biofilm formation on a urethral catheter is deposition of a conditioning film of host urinary components, including proteins, electrolytes, and other organic molecules [8]. Free-flowing bacteria attach to the surface through hydrophobic and electrostatic interactions and through the use of flagella where they form a self-organised cooperative community with high resistance to antimicrobial treatment [8, 9]. Intracellular communication by quorum sensing regulates the formation of such three-dimensional communities forming a biofilm which cannot be removed by simple shear forces and offers good growing conditions for other free-flowing bacteria. This leads to clogging of the catheter lumen and promotes bacterial colonisation. The resistance of bacteria inhabiting the biofilm can be up to thousand times higher when compared to free-flowing bacteria in urine [6, 9, 10]. In addition to biofilm clogging, the bacteria *Proteus mirabilis* causes clogging and encrustation of the catheter by precipitation and adsorption of calcium and magnesium phosphate present in urine. Long-term use of indwelling catheters results in salt encrustation in 50% of the cases [11, 12]. In some cases, an excess of proteins can also be present in the urine which additionally contributes to fouling of the urethral catheter. The presence of excess protein in urine is referred to as proteinuria. So far, there is no evidence that would directly link UTI as the cause for proteinuria [13], but many patients who need catheterisation develop proteinuria

due to the nature of their medical state, such as people who suffer from spinal cord injuries [14]. Because of the latter and the role of proteins in the biofilm formation, their presence must be taken into consideration when developing antimicrobial and antifouling urethral catheters.

Overcoming these problems is the driving force for the development of surface-modified bioactive urethral catheters. New trends, including coatings specifically targeting bacterial deposition, natural polymer coatings, enzyme active coatings or biomolecular coatings, are slowly replacing conventional antibiotic treatments and metal ion coatings [15].

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