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Research Paper

Reduction of *Staphylococcus aureus* and *Pseudomonas aeruginosa* colonisation on PVC through covalent surface attachment of fluorinated thiols

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Abstract

Objectives This study reports the development, characterisation and microbiological testing of surface-modified polyvinylchloride (PVC) films for the purpose of reducing bacterial adherence.

Methods Irreversible covalent surface modification was achieved via nucleophilic substitution of fluorinated thiol-terminated compounds onto the polymer backbone. Four fluorinated modifiers, 2,3,5,6-tetrafluorothiophenol (TFTP), 4-(trifluoromethyl)thiophenol (TFMTP), 3,5-bis(trifluoromethyl)benzenethiol (BTFMBT) and 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol (HDFDT), were investigated. Modification was confirmed using attenuated total reflectance infrared spectroscopy; Raman mapping demonstrated that modification was homogenous on the macroscopic scale. The influence of fluorination on surface hydrophobicity was studied by contact angle analysis. The effect on microbial adherence was examined using *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Key findings The resultant changes in contact angle relative to control PVC ranged from –4° to +14°. In all cases, adherence of *P. aeruginosa* and *S. aureus* was significantly reduced relative to control PVC, with adherence levels ranging from 62% and 51% for TFTP-modified PVC to 32% and 7% for TFMTP-modified PVC.

Conclusions These results demonstrate an important method in reducing the incidence of bacterial infection in PVC medical devices without compromising mechanical properties.

Keywords bacterial adhesion; contact angle; infrared spectroscopy; polyvinylchloride; Raman spectroscopy; surface modification

Introduction

Polyvinylchloride (PVC) is one of the most widely used polymers in healthcare, accounting for more than 25% of all medical polymers used in hospitals.[1] In particular, it is an important biomaterial used in the manufacture of medical devices such as the endotracheal (ET) tube. ET tubes are used in airway management and mechanical ventilation of patients incapable of breathing unassisted and, as such, are life-saving pieces of equipment. However, as with all implanted biomaterials, PVC is prone to bacterial colonisation, which can lead to the formation of highly antibiotic-resistant biofilms, often resulting in infection in the surrounding tissue.[2] This is a serious complication in the case of PVC ET tubes, leading to ventilator-associated pneumonia (VAP), which results in significant patient morbidity and mortality.[3]

Previous attempts to reduce the incidence of infection of implanted PVC biomaterials have explored a variety of methods, including the use of antimicrobial and anti-adherent coatings, and the incorporation of antimicrobial agents directly into the device.[4–6] These strategies have had limited success, principally because of issues relating to poor mechanical performance of either the coating or the impregnated device, or inappropriate drug elution profiles.[5,7] These issues can potentially be overcome through appropriate chemical surface modification of PVC to yield anti-infective materials.

One of the most important considerations when dealing with PVC modification is the need to maintain the mechanical properties necessary for the material to function *in situ*, while improving the resistance of the device to infection.[5,8] With this in mind, attempts

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have been made at surface-only modification that would enable devices to retain their bulk properties while showing enhanced resistance to infection.

Much of the reported work in surface modification involves grafting polymers or organic species onto PVC by a variety of methods, including UV or ionising radiation and low-temperature plasma.[7] Plasma modification has been used to yield inherently anti-infective surfaces and also as a carrier for secondary anti-infective molecules, both of which have been shown to reduce adhesion of a variety of bacterial isolates.[9–11] As plasma-modified material begins to deteriorate after 10 days, however, and is relatively expensive, this approach has found limited clinical use.[11] Recent work has demonstrated the potential for controlled surface modification of PVC by nucleophilic substitution of a modifying agent onto the polymer backbone, a process that has been shown, with certain modifiers, to produce moderate reductions in bacterial adhesion.[12,13] Despite this, no approach offers clinically significant reductions in bacterial adhesion.[14]

In the natural world, the leaves of plants such as the lotus (*Nelumbo nucifera*) display self-cleaning behaviour via formation of high-contact-angle, essentially superhydrophobic, surfaces.[15] Recently, synthetic mimics of this 'lotus effect' have been achieved by the creation of low-surface-energy materials, such as those with a high degree of fluorination, and have been shown to be capable of resisting protein adhesion and bacterial adherence, which is relevant to the initial stages of biofilm formation.[16–20] We therefore investigated the surface modification of PVC with highly fluorinated organic molecules (Figure 1). Here we report the characterisation of the surface and bulk PVC thus modified and investigate the ability of the novel material surfaces to resist microbial adherence.

Materials and Methods

Unplasticised PVC films of 0.2 mm thickness were supplied by Goodfellow Cambridge Ltd (Cambridge, UK). 3,5-Bis (trifluoromethyl)benzenethiol (BTFMBT), 2,3,5,6-tetrafluorothiophenol (TFTP) and 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol (HDFDT) were purchased from Fluorochem (Old Glossop, UK) and 4-(trifluoromethyl)thiophenol (TFMTP) was from Apollo Scientific Ltd (Stockport, UK). All modifying agents were used without further purification. *N*,*N*-Dimethylformamide (DMF) and diethyl ether (spectroscopic grade) and potassium carbonate (99.9%) were obtained from VWR International (Lutterworth, UK).

Modification of unplasticised PVC films

Modification of PVC was achieved by modification of the method of Sacristán Mijangos *et al.*[12] A section of PVC film (3 × 3 cm) was immersed in a mixture of DMF/water (5 : 1 v/v, 100 ml) and modifying agent (10 mmol TFTP, TFMTP or BTFMBT, or 5 mmol HDFDT) with potassium carbonate (1 equivalent), and held at 60°C for 6 h. The modified PVC sample was washed thoroughly with deionised water. To remove any remaining modifier and solvent, samples were washed in diethyl ether (100 ml) for 24 h, rinsed with diethyl ether (100 ml) and dried under vacuum before use.

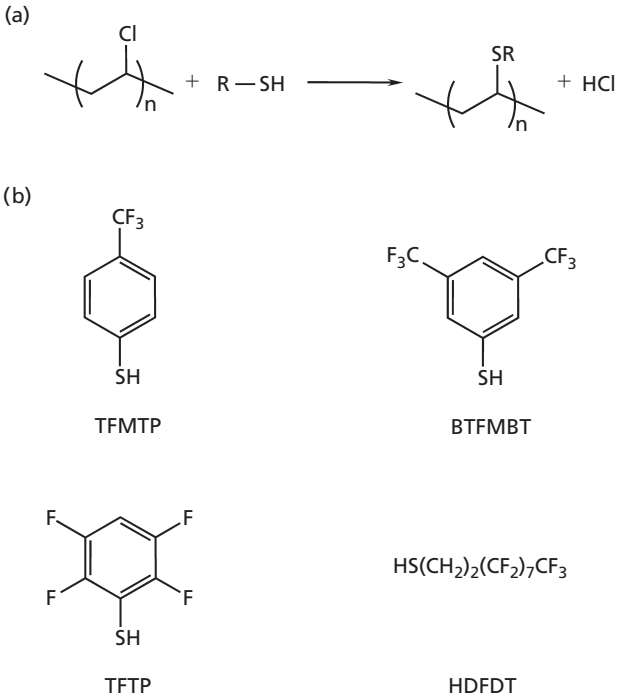

Figure 1 (a) Reaction of thiol-containing modifier with PVC. (b) Chemical structures of modifiers: 4-(trifluoromethyl)thiophenol (TFMTP), 3,5-bis(trifluoromethyl)benzenethiol (BTFMBT), 2,3,5,6-tetrafluorothiophenol (TFTP) and 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol (HDFDT).

Spectroscopic characterisation of modified PVC films

Materials were characterised by Fourier transform infrared (FTIR) and Raman spectroscopy. Attenuated total reflectance (ATR) FTIR spectra were collected using an FT/IR-4100 spectrometer (Jasco, Great Dunmow, UK) equipped with a Pike MIRacle ATR accessory with diamond crystal. Spectra are an average of 16 scans at a resolution of 4 cm^{-1}. Infrared spectra of pure modifying agents were collected by placing one drop between two potassium bromide windows and taking an average of 10 scans at a resolution of 4 cm^{-1}. Raman maps were obtained using a RamanStation R3 (Avalon Instruments, Belfast, UK) coupled to a motorised stage. Raman scattered light from a 785 nm laser operating at 300 mW was collected between 400 and 3200 cm^{-1} at a resolution of 2 cm^{-1}, and with a total collection time of 20 s. Maps were created by collecting 100 adjacent spectra at 100 μm intervals in a 10 × 10 grid (total coverage 0.9 mm^2) and analysed using Avalon Instruments Insight software, using a laser spot size of 150 μm. A z-stage autofocus adjustment was made before collecting each spectrum to normalise intensities.

Static contact angle analysis of modified PVC samples

Static contact angles were determined for 15 replicate samples of each material by measuring the angle formed by a single drop of water on the sample using an FTA200

dynamic contact analyser (First Ten Angstroms, Portsmouth, VA, USA) fitted with video capture camera. Image capture and analysis was enabled using FTA32 video software.

Microbial adherence study

Pseudomonas aeruginosa (Gram-negative) and *Staphylococcus aureus* (Gram-positive) were used as models for in-vivo microbial adherence. *P. aeruginosa* and *S. aureus* are the causative organisms in a significant number of cases of VAP, and are associated with high mortality.[21–23] Clinical isolates of *P. aeruginosa* (PAO1 NCIMB 10548) and *S. aureus* (P71 B1) were prepared by inoculation into separate tubes of pre-warmed Müeller Hinton broth (Davidson & Hardy Laboratory Supplies Ltd., Belfast, UK) and incubating at 37°C for 18 h, after which the bacterial suspension was centrifuged at 3000 rpm for 15 min and the resultant bacterial pellet resuspended in a volume of phosphate-buffered saline (pH 7.4) to yield an optical density of 0.9 at 540 nm (approximately 1×10^8 cfu/ml). The actual inoculum size determined by viable count was 5.5×10^6 cfu/ml for *P. aeruginosa* and 7.0×10^8 cfu/ml for *S. aureus*.

Test samples were prepared by removing discs of equal surface area using a steel borer (10 mm diameter) from the materials and mounting on hypodermic needles. Enough inoculum was added to each of five replicate samples of each material to ensure complete coverage of the samples, which were placed in an orbital incubator at 37°C for 24 h. Following incubation, the samples were removed and washed three times with quarter-strength Ringer's solution (QSRS) to remove non-adherent bacteria. The samples were transferred into fresh QSRS and sonicated for 5 min, followed by vortex mixing for 30 s. To determine the number of adhered bacteria, a viable count of the QSRS was performed using Müeller Hinton agar.

Statistical analysis

For all replicated measurements, at least five replicate measurements were obtained and values are expressed as means ± SD. The effects of modification on contact angle and microbial adherence were assessed for statistical significance using one-way analysis of variance; post-hoc comparisons were made using Tukey's HSD test. Significance was denoted by $P < 0.05$.

Results

PVC was reacted with a series of terminal thiols through nucleophilic substitution of the C–Cl group of PVC by a preformed thiolate in a DMF/water mixture (Figure 1a), which limits penetration of the thiols into bulk PVC but allows surface reaction. A series of thiols, TFMTP, BTFMBT, TFTP and HDFDT (Figure 1b), which show a range of steric geometries and degrees of fluorination, were reacted separately with PVC.

Infrared spectroscopic characterisation of modified PVC surfaces

Overlaid ATR IR spectra of unmodified (control) PVC and PVC modified with TFTP, BTFMBT, TFMTP or HDFDT between 1500 and 1000 cm^{-1} are shown in Figure 2. Spectra of materials modified with thiols all show distinct changes compared with control PVC resulting from the presence of covalently bound modifiers at the material surface.

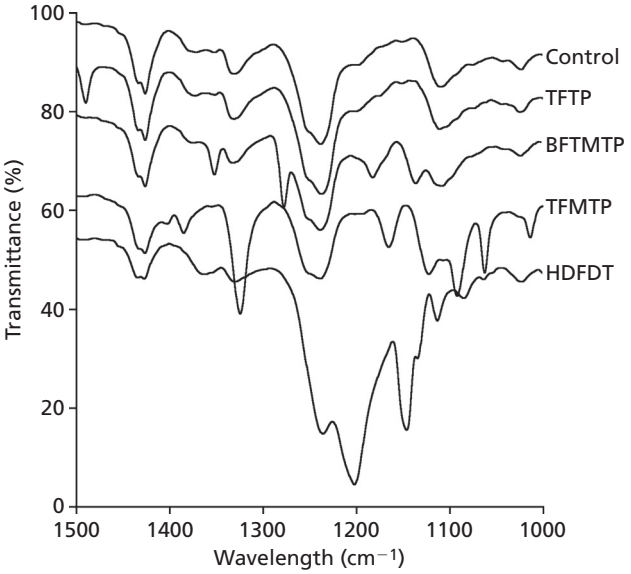

Figure 2 Attenuated total reflectance FTIR spectra (1500–1000 cm^{-1}) of unmodified PVC and samples reacted with thiol-containing modifying agents. TFTP, 2,3,5,6-tetrafluorothiophenol; BFTMTP, 3,5-bis(trifluoromethyl)thiophenol; TFMTP, 4-(trifluoromethyl)thiophenol; HDFDT, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol.

TFTP-modified PVC shows a number of new bands compared with unmodified PVC that are also present in the spectrum of pure TFTP, including a band forming at 1490 cm^{-1}, indicating the presence of a fluorinated aromatic ring, and a lower intensity band at 1172 cm^{-1}, ascribed to a C–F stretching mode of vibration.[24,25] Bands corresponding to aromatic C–H bending modes of attached TFTP were observed at 916, 891 and 835 cm^{-1}.[25] A large shoulder at 710 cm^{-1} and new bands at 628 and 617 cm^{-1} are ascribed to the aryl and alkyl thioether bonds, respectively,[24] indicating covalent reaction with PVC.

BTFMBT-modified PVC shows several bands not observed in control PVC; bands at 1353, 1185 and 1139 cm^{-1} indicate C–F stretches of trifluoromethyl groups, and a band at 1279 cm^{-1} is associated with the aromatic ring of BTFMBT.[26] Bands at 713 and 654 cm^{-1} are assigned to an aromatic and an aliphatic C–S bond, respectively.[24,25] These bands were also observed in pure BTFMBT with the exception of the aliphatic C–S band, which evolved only on covalent attachment to PVC.

Spectral differences were observed between TFMTP-modified PVC and control PVC. A C–F stretching band was observed at 1325 cm^{-1},[25] and bands associated with the aromatic ring were observed at 1167 and 1610 cm^{-1}.[26] Confirmation of covalent bonding to PVC was obtained from a band attributed to an aliphatic thioether group at 628 cm^{-1}, which is not observed in the spectrum of pure TFMTP.

HDFDT-modified PVC shows similar changes to TFMTP, with new bands observed at 1237, 1147, 1135, 1114 and

1063 cm^{-1} resulting from a variety of C–F vibrations on the fluorinated alkyl chain.[25,27] A sharpening and increase in intensity of bands at 628 and 612 cm^{-1} indicates covalent thioether bonding to PVC; these bands were absent from the spectrum of pure HDFDT.

Raman spectroscopic characterisation of modified PVC surfaces

Both control PVC and the modified samples were mapped using Raman spectroscopy in conjunction with a motorised stage. False-colour maps were produced using data obtained from the collected spectra, with shades of green representing intensity of a band due exclusively to PVC and shades of red representing intensity of a band due exclusively to the modifier. A colour look-up table which gives good contrast across the intensities measured was selected to emphasise small differences in intensities. The results of mapping of control and HDFDT-modified PVC samples are shown in Figure 3. The band between 860 and 880 cm^{-1}, with a band maximum at 866 cm^{-1} and identified as altered aliphatic C–C vibrations of the modified PVC backbone, was chosen to indicate the presence of HDFDT at the surface, while the band in the range 820–860 cm^{-1}, corresponding to similar vibrations in the absence of modification, was chosen as a band specific to PVC.[28,29] The shades of green and red determined at each map point together give an indication of the homogeneity and degree of surface modification. Figure 3a shows unmodified PVC as a homogeneous, predominantly green map, indicating the presence of only PVC. By contrast, Figure 3b shows almost complete homogeneous surface coverage of HDFDT on the HDFDT-modified PVC sample. Similar results were obtained for TFTP- and TFMTP-modified samples, surface modification being homogenous in both cases. Maps of BTFMBT-modified PVC could not be obtained because of sample fluorescence. The resolution obtained by this method demonstrates that there is no macrophase separation.

Effects of surface modification on static contact angle of PVC

The effects of surface modification were initially examined by measuring the static contact angle of water with control PVC and modified samples. The contact angles determined for the materials are presented in Table 1. The largest change in contact angle was measured for HDFDT-modified PVC (+13.5°), with similar increases in contact angle increases for TFMTP-modified PVC (+10.6°) compared with control PVC. TFTP- and BTFMBT-modified samples exhibited reduced contact angles compared with control PVC.

Effects of surface modification on microbial adhesion on PVC

The effect of surface modification on microbial adhesion was determined by challenging samples with *P. aeruginosa* and *S. aureus* inoculi of 5.5×10^6 and 7.0×10^8 cfu/ml, respectively, over 24 h. The adherence of microorganisms is shown in Figure 4, which indicates that, in all cases, surface modification of PVC reduces the adherence of both *S. aureus* and *P. aeruginosa* compared with control PVC. Statistical analysis showed significant reductions in the number of adherent bacteria relative to the control for TFMTP- and HDFDT-modified PVC samples. BTFMBT-modified PVC also exhibits a statistically significant reduction in adherence

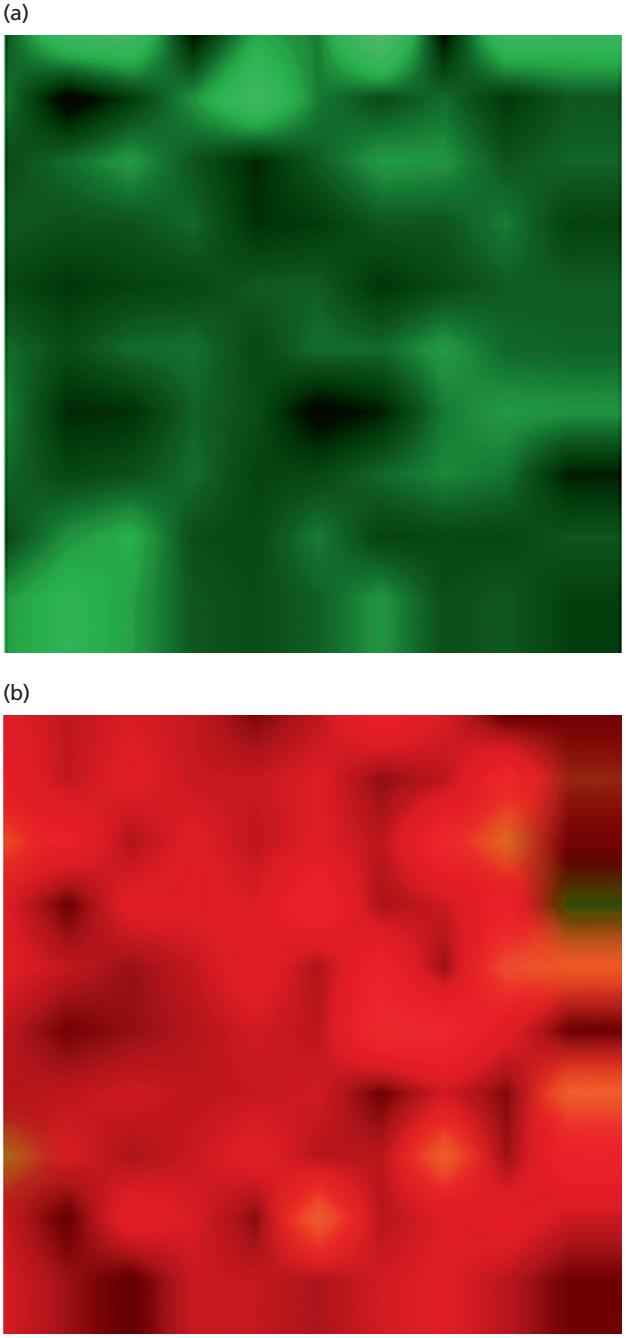

Figure 3 Raman maps comparing relative band areas of a HDFDT-specific band (880–860 cm^{-1}) and a PVC-specific band (860–820 cm^{-1}), showing the extent of surface modification of (a) unmodified control PVC and (b) HDFDT-modified PVC. Areas of unmodified and HDFDT-modified PVC are shown in shades of green and red respectively, with colour brightness representing intensity. Each map represents an area of 0.9 × 0.9 mm. HDFDT, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol.

Table 1 Static contact angles of unmodified control PVC and PVC modified with various thiol-containing modifiers

Modifier	Contact angle (°)
Control	75.6 ± 2.70
TFTP	71.7 ± 5.53
TFMTP	86.2 ± 3.90
BTFMBT	71.0 ± 6.11
HDFDT	89.1 ± 3.96

Values are means ± SD (n = 15). TFTP, 2,3,5,6-tetrafluorothiophenol; BFTMTP, 3,5-bis(trifluoromethyl)thiophenol; TFMTP, 4-(trifluoromethyl)-thiophenol; HDFDT, 3,3,4,4,5,5,6,6,7, 7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol.

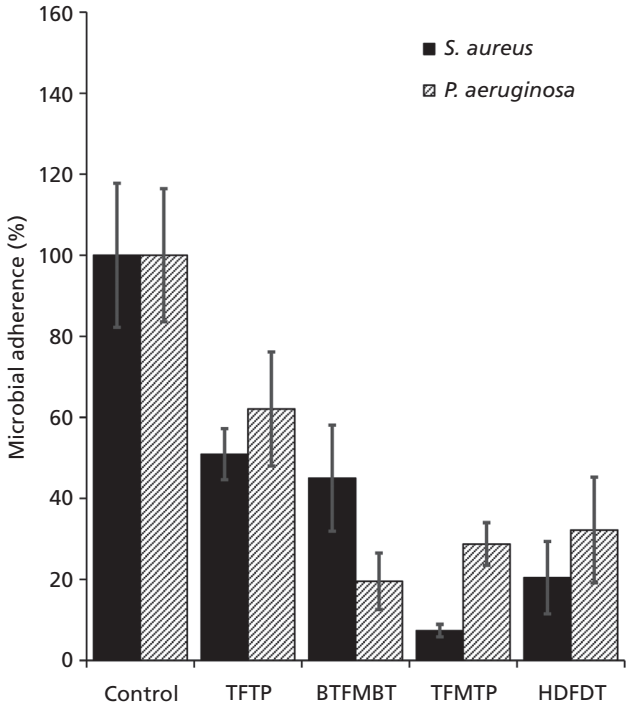

Figure 4 Microbial adherence of *P. aeruginosa* and *S. aureus* after 24 h to unmodified control and TFTP-, BTFMBT-, TFMTP- and HDFDT-modified PVC samples, relative to untreated PVC, denoted control (%). Columns and error bars represent means ± SD (n = 5). TFTP, 2,3,5,6-tetrafluorothiophenol; BFTMTP, 3,5-bis(trifluoromethyl)thiophenol; TFMTP, 4-(trifluoromethyl)thiophenol; HDFDT, 3,3,4,4,5,5,6,6,7, 7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol.

of *P. aeruginosa* compared with control PVC. The reduction in bacterial adherence to TFTP-modified PVC was not significant. Control PVC showed an identical number of adherent organisms to untreated PVC. The material that most successfully reduced adherence was that modified using TFMTP, with the average number of bacteria adhering reduced to 32.2% (*P. aeruginosa*) and 7.4% (*S. aureus*) of that on untreated PVC. HDFDT-modified materials showed similar significant reductions in bacterial adherence of 28.7% and 20.5%, respectively, compared with untreated PVC, while modification using BTFMBT resulted in reductions of *P. aeruginosa* adherence to 19.5%. TFTP-modified PVC was the least effective sample at reducing bacterial adherence, although reductions of 62.1% and 50.9% were still observed.

Discussion

The reaction of PVC with a preformed thiolate has been shown to be a clean reaction with no side products.[8] In this study, the use of a DMF/water mixture limited penetration of the thiols into bulk PVC but allowed surface reaction of TFMTP, BTFMBT, TFTP and HDFDT. The degree and homogeneity of the reaction, and the reactions at the PVC surface were characterised using infrared and Raman spectroscopy. To clearly characterise the reaction of thiols with PVC, unplasticised polymer was used. The majority of PVC used in medical device applications is, however, plasticised. All commonly used plasticisers are chemically inert towards thiols, so we expect our results to translate readily to device materials.

ATR FTIR and Raman spectroscopy are complementary techniques, which together allow characterisation of the surfaces of modified samples, allowing the progress of the modification reaction to be evaluated.[25] Infrared spectra of the modified samples showed several differences from control PVC. The majority of these changes correlated with the spectra of the relevant pure modifying agent and corresponded to key functional groups, such as the aromatic rings of TFTP, BTFMBT and TFMTP, and the C–F bonds present in all the modifiers.[25] Of particular interest in this respect are the presence and absence of two bands: firstly, a band corresponding to an aliphatic C–S bond that was not associated with the pure modifier but was observed for all modified samples between 617 and 654 cm^{-1}, and, secondly, the absence of a band centred at 2600 cm^{-1}, where the band attributable to the thiol group is found in the spectra of the pure modifiers. These differences together indicate covalent attachment of the thiol group to PVC, resulting in the formation of a thioether bond, for each of the thiol-containing modifiers used.

Raman spectroscopy identified significant changes in the energy associated with C–C vibrations of the PVC backbone, due to changes in the environment of these bonds resulting from substitution of the strongly electronegative chlorine atom in PVC with the thiol modifier to form a thioether bond containing the less-electronegative sulfur, causing a shift to higher frequencies.[25,30] Raman spectroscopy is particularly sensitive to changes in the energy associated with the vibrational modes of C–C bonds in the PVC backbone, which have low dipole moment and hence give rise to inherently weak FTIR signals, but which are polarisable. Since modification of the entire surface was not achieved, both modified and unmodified regions are present and bands corresponding to both are observed. The ratio of these bands enables qualitative determination of both the extent and homogeneity of surface modification through Raman mapping. Using the bands at 860–820 cm^{-1}, representing an unmodified PVC band, and 880–860 cm^{-1}, representing a modified PVC band, a map was constructed of the HDFDT-modified surface. The colour and brightness of the map show

the extent and homogeneity of the modification. As shown in Figure 3, HDFDT-modified PVC was significantly modified in a largely homogenous manner. The mapping process indicated that modification occurred to a lesser extent with TFMTP than with HDFDT, and that coverage is less homogenous, while use of TFTP led to a surface with minimal modification. Mapping of BTFMBT-modified PVC proved unsuccessful because of auto-fluorescence of the sample.

Contact angle analysis allows characterisation of the manner in which the modifiers affect the surface of PVC. Samples exhibiting largely homogenous surface modification (TFMTP- and HDFDT-modified samples) exhibited increases in contact angle compared with control PVC. Conversely, samples that showed less homogeneity in Raman mapping exhibited decreases in contact angle. There may therefore be a minimum degree of surface modification that allows sufficient homogeneity of surface modification to create more hydrophobic PVC surfaces. It also surprising that there are no significant differences in contact angle measurements between HDFDT and TFMTP, even though HDFDT is a much more highly fluorinated molecule. This demonstrates that, in accordance with previous studies of the lotus effect, hydrophobicity is not due to the chemical groups present on the surface alone, but also to the positioning of these groups and of the molecule as a whole, and the physical topography these create on the surface.[18] Even though the modified materials would be expected to have a lower surface energy than PVC through fluorination,[18] this parameter does not control the observed surface hydrophobicity.

Ultimately, the success of this approach is determined by the impact that surface modification has on microbial adherence. This was assessed by incubating the sample with *P. aeruginosa* (Gram-negative) and *S. aureus* (Gram-positive) organisms, which are implicated in the pathogenesis of VAP associated with the use of PVC ET tubes. The study was carried out in a non-proteinaceous medium so that the effect of adherence in the absence of conditioning film could be examined, which is a reasonable model for luminal ET tube biomaterials. All modified samples showed greater resistance to bacterial adherence after 24 h than unmodified control PVC. This may be due to surface energy effects, where adhesion events are inhibited, and/or proliferation effects, where biofilm development is inhibited. We are examining the effect of surface fluorination on both of these. The reduction in adherence after 24 h indicates that both primary adherence and subsequent biofilm formation are inhibited by the presence of fluorinated surface thiols. While biofilm is not eradicated using this method alone, the results demonstrate that its development is significantly retarded. This may prove clinically useful in combination with current clinical practices such as chlorhexidine lavage. The results demonstrate that increasing the contact angle significantly reduces bacterial adherence, as demonstrated by TFMTP-modified samples (68% for *P. aeruginosa* and 93% for *S. aureus*) and HDFDT-modified samples (71% and 80%, respectively), and that the higher the angle, the greater the effect. However, decreasing the contact angle, as with TFTP- and BTFMBT-modified samples, also decreases adherence (50% and 85% respectively). The unmodified control PVC exhibited comparable adherence to PVC, despite a significant reduction in contact angle, showing that processing of the sample is not responsible for the reduced adherence observed on modified PVC samples. As the adhesion of bacteria at polymeric surfaces depends on surface energy, surface topography and the cell attachment mechanism,[31] our results show that lowering the surface energy through fluorination is effective; greater control of surface organisation phenomena may enhance the reductions further.

Conclusions

This study presents a method for the covalent attachment of a range of thiol modifiers to PVC biomaterial surfaces using mild reaction conditions. The modification reaction can be effectively characterised using FTIR and Raman spectroscopy, and the homogeneity of surface modification can be characterised using Raman mapping. The materials produced have modified static contact angles with respect to PVC and are capable of resisting colonisation by both *P. aeruginosa* and *S. aureus*, implicated in ET tube colonisation and VAP. Both the nature of the modifier used and the homogeneity of surface modification affect both the contact angle and changes in microbial adherence; sterically uncrowded fluorinated thiols were particularly effective at reducing adherence. Importantly, the fluorinated surface acts without adversely affecting the bulk mechanical properties of the underlying PVC material. These results will inform the development of a subsequent generation of surface-modified PVC materials, with the goal of reducing the incidence of VAP and related conditions resulting from infection of PVC biomaterial surfaces.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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References

1. Tickner JA *et al*. Health risks posed by use of di-2-ethylhexyl phthalate (DEHP) in PVC medical devices: A critical review. *Am J Ind Med* 2001; 39: 100–111.

2. Adair CG *et al*. Implications of endotracheal tube biofilm for ventilator-associated pneumonia. *Intensive Care Med* 1999; 25: 1072–1076.
3. Safdar N *et al*. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005; 33: 2184–2193.
4. Darouiche RO. Anti-infective efficacy of silver-coated medical prostheses. *Clin Infect Dis* 1999; 29: 1371–1377.
5. Jones DS *et al*. Physicochemical characterization of hexetidine-impregnated endotracheal tube poly (vinyl chloride) and resistance to adherence of respiratory bacterial pathogens. *Pharm Res* 2002; 19: 818–824.
6. Jones DS *et al*. Characterisation and evaluation of novel surfactant bacterial anti-adherent coatings for endotracheal tubes designed for the prevention of ventilator-associated pneumonia. *J Pharm Pharmacol* 2003; 55: 43–52.
7. Ikada Y. Surface modification of polymers for medical applications. *Biomaterials* 1994; 15: 725–736.
8. Navarro R *et al*. Modification of poly (vinyl chloride) with new aromatic thiol compounds. Synthesis and characterization. *Polym Degrad Stab* 2008; 93: 585–591.
9. Balazs DJ *et al*. Surface modification of poly(vinyl chloride) intubation tubes to control bacterial adhesion: Teflon-like and Pluronics. *Eur Cell Mater* 2002; 3(Suppl. 1): 7–8.
10. Triandafillu K *et al*. Adhesion of Pseudomonas aeruginosa strains to untreated and oxygen-plasma treated poly(vinyl chloride) (PVC) from endotracheal intubation devices. *Biomaterials* 2003; 24: 1507–1518.
11. Zhang W *et al*. Plasma surface modification of poly vinyl chloride for improvement of antibacterial properties. *Biomaterials* 2006; 27: 44–51.
12. Sacristán J *et al*. Surface modification of PVC films in solvent–non-solvent mixtures. *Polymer* 2000; 41: 5577–5582.
13. Herrero M *et al*. Controlled wet-chemical modification and bacterial adhesion on PVC-surfaces. *Polym Degrad Stab* 2006; 91: 1915–1918.
14. Roosjen A *et al*. Inhibition of adhesion of yeasts and bacteria by poly(ethylene oxide)-brushes on glass in a parallel plate flow chamber. *Microbiology* 2003; 149: 3239–3246.
15. Cheng YT *et al*. Effects of micro-and nano-structures on the self-cleaning behaviour of lotus leaves. *Nanotechnology* 2006; 17: 1359–1362.
16. Tsibouklis J *et al*. Preventing bacterial adhesion onto surfaces: the low-surface-energy approach. *Biomaterials* 1999; 20: 1229–1235.
17. Pagliaro M, Ciriminna R. New fluorinated functional materials. *J Mater Chem* 2005; 15: 4981–4991.
18. Tsibouklis J *et al*. Poly (perfluoroalkyl methacrylate) film structures: surface organization phenomena, surface energy determinations, and force of adhesion measurements. *Macromolecules* 2000; 33: 8460–8465.
19. Kawakami H *et al*. Albumin adsorption to surface of annealed fluorinated polyimide. *Polym Adv Technol* 2001; 12: 244–252.
20. Zhang X *et al*. Superhydrophobic surfaces: from structural control to functional application. *J Mater Chem* 2008; 18: 621–633.
21. Rello J *et al*. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. *Chest* 2002; 122: 2115–2121.
22. Kollef MH *et al*. Clinical cure and survival in Gram-positive ventilator-associated pneumonia: retrospective analysis of two double-blind studies comparing linezolid with vancomycin. *Intensive Care Med* 2004; 30: 388–394.
23. Crouch Brewer S *et al*. Ventilator-associated pneumonia due to Pseudomonas aeruginosa. *Chest* 1996; 109: 1019–1029.
24. Robson P *et al*. Aromatic polyfluoro-compounds. Part VI. Penta- and 2, 3, 5, 6-tetra-fluorothiophenol. *J Chem Soc* 1960: 4754–4760.
25. Coates JP. Interpretation of infrared spectra, a practical approach. In: Meyers RA, ed. *Encyclopedia of Analytical Chemistry*, 1st edn. Chichester: John Wiley & Sons, 2000: 10815–10837.
26. Kang JF *et al*. Mixed self-assembled monolayers of rigid biphenyl thiols: impact of solvent and dipole moment. *J Am Chem Soc* 1998; 120: 9662–9667.
27. Ishikawa Y *et al*. Self-assembly of bilayers from double-chain fluorocarbon amphiphiles in aprotic organic solvents: thermodynamic origin and generalization of the bilayer assembly. *J Am Chem Soc* 1994; 116: 5579–5591.
28. Patnaik P. *Dean's Analytical Chemistry Handbook*, 2nd edn. New York: McGraw-Hill Professional, 2004.
29. Smith E, Dent G. *Modern Raman Spectroscopy: a Practical Approach*, 1st edn. Chichester: Wiley, 2005.
30. Mayo DW *et al*. *Course Notes on the Interpretation of Infrared and Raman Spectra*, 1st edn. Hoboken: Wiley-Interscience, 2003.
31. Cunliffe D *et al*. Bacterial adhesion at synthetic surfaces. *Appl Environ Microbiol* 1999; 65: 4995–5002.