Sequential polyurethane–poly(methylmethacrylate) interpenetrating polymer networks as ureteral biomaterials: mechanical properties and comparative resistance to urinary encrustation

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The mechanical properties and resistance to urinary encrustation of sequential-interpenetrating polymer networks (IPNs) composed of polyurethane (PU) and polymethylmethacrylate (PMMA), have been described. Mechanical properties were determined using tensile testing and dynamic mechanical analysis, whereas resistance to encrustation was examined using an *in vitro* model for encrustation simulating *in vivo* encrustation. Maximum and minimum tensile strength at break, Young's modulus, storage and loss moduli were associated with PMMA and PU, respectively. IPNs demonstrated intermediate mechanical properties which were dependent on the concentrations of the component polymers. Conversely, maximum elongation at break was observed for PU and this parameter decreased as the concentration of PMMA increased in the IPN. The dynamic mechanical damping parameter, tan δ, was similar for all IPNs at 37 °C. Increased advancing and decreased receding contact angles were observed for IPNs in comparison with the native PU. The rate and extent of encrustation, measured as the percentage surface coverage, was similar for PU, IPNs and PMMA. In contrast, encrustation on polyhydroxyethylmethacrylate, a model hydrogel, was greater than observed for the IPNs or component polymers. No apparent correlation was observed between the rate and/or extent of encrustation and polymer contact angle. It is concluded that these IPNs may be of clinical benefit in patients providing stent resistance to extrinsic compression of the ureter in comparison with native PU. The comparable resistance to encrustation between the IPNs and PU indicates that the use of IPNs should not be restricted in this regard.

1. Introduction

Ureteral stents are synthetic polymeric biomedical devices which are employed to provide internal upper urinary tract drainage whenever there is obstruction of urinary flow [1, 2]. Indications for their use include, obstructive uropathy, primary or malignant carcinomas, radiation fibrosis or retroperitoneal fibrosis [2, 3]. The duration of ureteral stenting may range from a few days to many months and furthermore, patients with complex problems may require extended use of stents [1]. However, over the past three decades the use of ureteral stents has had associated problems, including infection, encrustation and fracture [2, 4–6]. The rate of encrustation onto ureteral stents is dependent on the polymeric composition of the stent and the chemical composition of the urine [2]. Consequently, manufacturers currently recommend that stent removal should occur after 3 months initially, and if no encrustation has occurred, thereafter at 6 month intervals [4, 7].

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Several different polymeric materials are currently employed as ureteral stents, including silicone, polyurethane, Silitek™ (a silicone-based copolymer), C-Flex™ (a silicone-modified thermoplastic elastomer) and Percuflex™ (a thermoplastic block copolymer) which, due to the diversity of design, exhibit a range of mechanical properties and also varied resistance to encrustation [5, 8]. Following assessment of material strength, coil retention, surface friction, biodurability and biocompatibility, Mardis *et al.* [8] reported that C-Flex™ and Percuflex™ are the most suitable materials for stent construction. In a more recent study, we examined the comparative resistance of silicone, polyurethane, Silitek™, Percuflex™ and a hydrogel-coated polyurethane to encrustation in an *in vitro* encrustation model [5, 9] and reported that silicone was the least prone to encrustation. Ureteral stents constructed with soft polymeric materials such as silicone or silicone-based copolymers are easily constricted in many patients, thereby restricting urine drainage. Rigid polymeric stents should be used in such patients [10]. Therefore, owing to the many demands required from ureteral stents, no one material currently exhibits all the required attributes for ideal clinical performance.

One method by which the mechanical properties of existing biomaterials may be improved is by the formation of interpenetrating polymer networks (IPNs). These are heterogenous systems containing two or more polymer networks consisting of physical entanglement of polymer chains that have been synthesized, either simultaneously or sequentially, with respect to each other [11–13]. The enhanced polymer rigidity which results from the formation of IPNs may, therefore, be useful in the design of ureteral stents for patients with extrinsic compression of the ureter. This study reports the mechanical and surface characterization of sequential interpenetrating networks composed of polyurethane, selected because of its versatility and low cost, and polymethylmethacrylate, a polymer which has been used in medical devices, for use in conditions where stent rigidity is required. In addition, the resistance of these IPNs to encrustation, a fundamental requirement of all ureteral stents, in an *in vitro* model is examined.

2. Materials and methods

2.1. Materials

Medical grade polyurethane (0.45 mm thick) was donated by Vas-Cath Inc. (Ontario, Canada). Methylmethacrylate, azobisisobutyronitrile and hydroxyethylmethacrylate were purchased from Sigma Chemicals (UK). All other chemicals were purchased from BDH Chemicals Ltd (UK) and were AnalaR, or equivalent, grade.

2.2. Synthesis of polymethylmethacrylate (PMMA) and polyhydroxyethylmethacrylate (PHEMA)

Inhibitor-free methylmethacrylate (MMA; 99.5% wt/wt) or hydroxyethylmethacrylate (HEMA; 99.5% wt/wt) were mixed with azobisisobutyronitrile (AIBN, 0.5% wt/wt). This solution (20 ml) was then syringed into a mould composed of two glass plates, which were separated by rubber spacers and clamped using spring clips. The mould was then placed in an oven at 60 °C for 18 h to allow polymerization. On removal from the oven, the polymethylmethacrylate (PMMA) or polyhydroxyethylmethacrylate (PHEMA) sheets were stored in a desiccator until required.

2.3. Preparation of sequential interpenetrating polymer networks (IPNs)

Strips of polyurethane (PU; 50 mm × 10 mm × 0.45 mm), which had previously been dried by storage in a vacuum oven at 40 °C for 24 h, were weighed and immersed in a solution composed of inhibitor-free MMA (99.5% wt/wt) and AIBN (0.5% wt/wt) for a range of times until the PU had achieved the required increase in weight. The strips were then removed from the MMA solution, blotted dry, located between two glass plates and incubated at 60 °C for 18 h to allow for polymerization of MMA. On removal from the oven, the IPNs were stored in a desiccator until required.

2.4. Mechanical testing of biomaterials

Tensile testing of PU, PMMA and IPN was performed using a Lloyd tensile tester (Lloyd Instruments, UK), according to ASTM D 638M-84, using a crosshead speed of 100 mm min^{-1}.

Dynamic mechanical analysis was performed using a Du Pont 983 dynamic mechanical analyser in fixed frequency mode over a temperature range of −60 to 70 °C at a heating rate of 4 °C min^{-1}. The amplitude (peak to peak) of sinusoidal oscillations was 1 mm and was selected according to the thickness and stiffness of the samples.

All mechanical analyses were performed at least in quadruplicate. In all cases, the coefficient of variation was less than 3% and consequently only the mean values of each analysis are shown in Section 3.

2.5. Dynamic contact angle measurement

The advancing and receding contact angles of PU, PMMA and IPN strips were determined in quadruplicate using a Dynamic Contact Angle Analyser (DCA 312, Cahn Instruments) at 25 °C. The wetting medium used was Reagent Grade 1 water from a Milli-Q system (Millipore UK, Ltd). In all cases the coefficient of variation was less than 3% and consequently only the mean values of each analysis are shown in Section 3.

2.6. Evaluation of *in vitro* encrustation

Resistance of PU, PMMA and IPN to encrustation was determined using the *in vitro* model previously described [9]. Five samples each of PU, PMMA and IPN were stored for specific periods in artificial urine

at 37 °C in an atmosphere consisting of 5% CO_2 in the encrustation model. Following this, the polymeric strips were removed and the percentage surface coverage with encrustation determined using fluorescence microscopy linked to an image analysis unit (Bio-Foss automated system 3, Foss-Electric UK Ltd, UK). In all cases, the coefficient of variation was less than 6% and therefore, to maintain clarity, only the mean percentage encrustation is illustrated.

2.7. Statistical analysis

Statistical comparisons of the mechanical properties, contact angles and rate and extent of encrustation of each biomaterial employed in this study were performed using a one-way analysis of variance ($p < 0.05$ denoting significance).

3. Results

The tensile properties of PU, PMMA and IPN are presented in Table I. Maximum and minimum ultimate tensile strength at break and Young's modulus were exhibited by PMMA and PU, respectively. Increasing percentage content of PMMA in the IPN increased force at break and Young's modulus, yet decreased percentage elongation at break compared with native PU.

Table II presents the dynamic mechanical analysis of PU, PMMA and the IPNs at 37 °C. The glass transition temperature, T_g, defined as the temperature of the maximum in tan δ, of PU was −25 °C and increased as the concentration of PMMA in the IPN increased. Maximum T_g was associated with pure PMMA. Similarly, as the content of PMMA was increased in the IPN, there were subsequent increases in the elastic modulus. However, there were no apparent differences between the tan δ of PMMA and the various IPNs.

TABLE III Advancing and receding contact angles of polyurethane (PU), polymethylmethacrylate (PMMA), polyurethane/polymethylmethacrylate (PU/PMMA) interpenetrating polymer networks and polyhydroxyethylmethacrylate (PHEMA)

Biomaterial (% wt/wt)	Advancing contact angle (deg)	Receding contact angle (deg)
PU 100%	77.09	77.80
PU 70%/PMMA 30%	89.83	38.23
PU 50%/PMMA 50%	93.93	47.01
PU 30%/PMMA 70%	89.82	47.40
PMMA 100%	98.61	55.49
PHEMA 100%	49.74	37.35

The advancing and receding contact angles of all biomaterials examined in this study are shown in Table III. Incorporation of PMMA into the IPNs significantly increased the advancing contact angle of the native PU. Similarly, addition of PMMA to PU resulted in significant reductions in the receding contact angles compared with PU. The maximum receding contact angle was associated with PU. As expected, the minimum advancing and receding contact angles were associated with PHEMA, 49.74° and 37.35°, respectively.

Fig. 1 shows the development of encrustation on each polymeric material with respect to time of immersion in artificial urine in the encrustation model. PHEMA demonstrated the greatest rate of encrustation (approximately 100% surface coverage after 2 wk). PU, PMMA and the IPNs exhibited total (100%) surface coverage after 4 wk. The rates of encrustation for PU, PMMA and the IPNs were statistically similar.

4. Discussion

Although there is a wide range of biomaterials available for use as ureteral stents, no one material exhibits

TABLE I Tensile properties of polyurethane (PU), polymethylmethacrylate (PMMA) and polyurethane/polymethylmethacrylate (PU/PMMA) sequential interpenetrating polymer networks (IPN) at ambient temperature

Composition of IPN (% wt/wt)	Mean ultimate tensile strength (MPa)	Mean elongation to failure (%)	Young's modulus of elasticity (GPa)
PU 100%	2.9	224.9	0.001
PU 70%/PMMA 30%	7.1	77.1	0.010
PU 50%/PMMA 50%	11.1	37.0	0.160
PU 30%/PMMA 70%	18.8	35.6	0.518
PMMA 100%	54.2	2.1	2.560

TABLE II Dynamic mechanical analysis of polyurethane (PU), polymethylmethacrylate (PMMA) and polyurethane/polymethylmethacrylate (PU/PMMA) interpenetrating polymer networks at 37 °C

Composition (% wt/wt)	Real modulus, E' (GPa)	Tan δ at 37 °C	Glass transition temperature (°C)
PU 100%	0.001	0.08	− 25
PU 70%/PMMA 30%	0.09	0.144	22
PU 50%/PMMA 50%	0.41	0.125	62
PU 30%/PMMA 70%	1.01	0.13	74
PMMA 100%	3.17	0.15	109

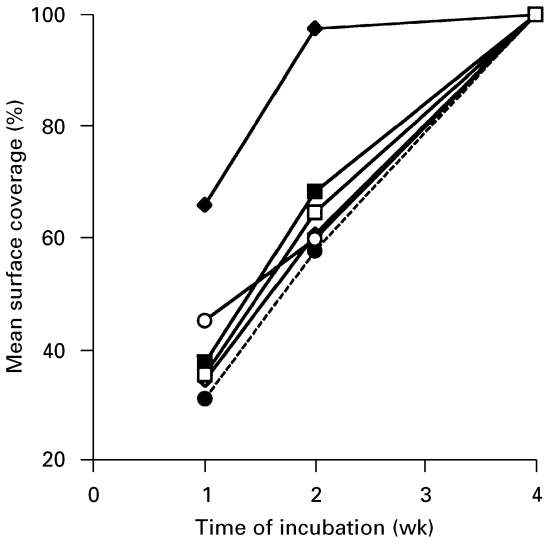

Figure 1 The effect of time of immersion of biomaterials in artificial urine on surface coverage (%) with encrustation. (□) Polyurethane (PU), (◇) polymethylmethacrylate (PMMA), (■) PU 70%/PMMA 30%, (○) PU 50%/PMMA 50%, (●) PU 30%/PMMA 70% and (◆) Polyhydroxyethylmethacrylate (PHEMA).

the ideal properties of resistance to urinary encrustation and possession of mechanical properties enabling both ease of insertion by the urologist and patient comfort *in situ* whilst maintaining urinary flow. This study was designed to enhance the mechanical properties of one of the most commonly used ureteral biomaterials, PU, to allow improved performance with particular emphasis on ease of insertion and maintanence of urinary drainage. IPNs are frequently employed to produce polymeric systems which demonstrate a wide range of mechanical properties [12, 13]. It has been reported that materials with enhanced properties can be produced by the formation of heterogeneous systems in which one polymeric component exists above (e.g. PU), and the other below (e.g. PMMA) their glass transition temperatures at the temperature to which the IPN will be exposed (e.g. 37 °C). The balance between these polymeric components determines the mechanical properties [11–13]. However, in spite of the obvious advantages of this approach, IPNs have not found extensive use as urinary biomaterials.

In this current study, we have produced a series of IPNs using PU and PMMA as the component polymers. The two component polymers demonstrated good compatibility, as evinced by the gradual increase in the T_g of the IPNs as the percentage of PMMA increased [12]. As predicted, the subsequent mechanical properties of the IPNs were dependent on the percentage of PMMA. As the content of the glassy component increased (PMMA), biomaterials were produced which displayed increased tensile strength, Young's modulus (rigidity) and dynamic moduli. These mechanical properties would, therefore, be expected to be advantageous for use in situations where increased mechanical performance is required, for example patients with suspected ureteric compression, as these IPNs would be less likely to undergo constriction or kinking [10]. The greater tan δ values of IPNs than PU at 37 °C (Table II) suggest that these materials possess a greater ability to dissipate applied stress.

It is imperative that new ureteral stent biomaterials demonstrate a resistance to encrustation. Failure to achieve this will render such biomaterials appropriate only for short-term use. Interestingly, PU, PMMA and various PU/PMMA IPNs demonstrated comparable encrustation to presently employed stent materials in our model. Therefore, it is likely that the IPNs will perform similarly to PU with respect to encrustation *in vivo*, as the *in vitro* model employed in this study has been shown to simulate *in vivo* encrustation [9]. The observed inability of PHEMA, a hydrogel, to resist encrustation in comparison to the other materials examined, was interesting as this polymer has been reported to resist encrustation in other studies. For example, Block *et al.* [14] reported no encrustation on the surface of PHEMA whenever used as a prosthetic ureter in the dog, whereas, Eckstein *et al.* [15] suggested that the ability of PHEMA to resist encrustation was due to the shrink–swell behaviour of this polymer whenever it is subjected to varying pH, as is often the case in the urinary tract. However, more recently it has been reported that hydrogel-coated catheters did not offer greater resistance to encrustation, both *in vitro* and *in vivo* [16–18]. This study has demonstrated a greater rate of surface encrustation of PHEMA in comparison to PU, PMMA and all IPNs. As encrustation involves interaction with the stent biomaterial surface, it is logical to assume that the properties of the biomaterial surface (e.g. contact angle) play an important role in this process affecting the thermodynamics of attachment between inorganic materials and the stent biomaterial. In this study, biomaterials were produced which exhibited a range of advancing and receding contact angles. The rate of encrustation appeared to be independent of either the advancing or receding contact angles of the biomaterials. PHEMA is a hydrophilic material and exhibited the lowest observed contact angles; however, at this stage it would be unwise to explain the increased rate of encrustation on the surface of PHEMA in terms of this surface property without further detailed examination. The IPNs and PMMA exhibited contact angle hysteresis, i.e. differences in the advancing and receding contact angles [19]. Whilst there may be several explanations for this phenomenon, as outlined by Andrade *et al.* [19], likely explanations may involve surface group reorientation, surface heterogeneity and/or penetration of water into the polymers with attendant swelling [20]. Rigid polymers have previously been associated with structural modifications, due to adsorbate interactions [21, 22], whereas heterogeneous surfaces, which are composed of areas of surface energy differing from the bulk surface, have been reported to exhibit contact angle hysteresis [19, 23].

5. Conclusion

The mechanical properties of the IPNs formed were shown to be dependent on their PU and PMMA composition. Increasing concentration of PMMA

resulted in increased tensile strength, Young's modulus, dynamic real modulus and glass transition temperature at body temperature. However, no apparent difference was observed between PMMA and the various IPNs with respect to tan δ. Increased advancing and decreased receding contact angles were associated with the inclusion of PMMA within the PU structure. The rate of encrustation was greatest for PHEMA while IPN, PU and PMMA all encrusted at a similar but considerably lower rate. Further studies would be of benefit to substantiate the conclusion that there is no relationship between biomaterial contact angle and rate of encrustation. However, the alterations to the mechanical properties of PU may be of clinical benefit in patients where enhanced mechanical properties are beneficial, for instance, where extrinsic compression of the ureter arises.

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