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In vivo biostability of polyurethane–organosilicate nanocomposites

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ABSTRACT

Organically modified layered silicates were incorporated into a polyether soft-segment polyurethane to form composites of at least delaminated morphology. The primary organic modifier was a quaternary ammonium compound; however, one composite included an alternative amino undecanoic acid-modified silicate. The composites' biostability was assessed in an in vivo ovine model over a period of 6 weeks. Attenuated total reflectance–Fourier transform infrared analysis and semi-quantitative scanning electron microscopy image rating indicate a significant enhancement of the base polyurethane biostability with the inclusion of silicate at 3 wt.%. The potential effect at 15 wt.% was confounded by probable leaching of the quaternary ammonium compound affecting the tissue response. The amino undecanoic acid composite compared favourably with the quaternary ammonium compound composite of equivalent silicate loading, and offers the promise of a more favourable tissue response.

1. Introduction

Polyurethane (PU) has, historically, been disadvantaged by having poor biostability in vivo. Such degradation is significant as it introduces a risk of loss of device function and/or compromised biocompatibility. Poly(ester)urethanes were among the earliest biomedical PUs. The problem of the ester's hydrolytic instability was initially addressed by poly(ether)urethanes (PEUs), but these have since been shown to be susceptible to degradation via oxidation of the ether linkages [1,2], and are thus currently limited to short-term applications in vivo. A PU originating from past work in our laboratory includes a polydimethylsiloxane (PDMS; $-(CH_3)_3-Si-O-[Si-O-(CH_3)_2]_n-Si-(CH_3)_3-$) soft segment and has significantly increased biostability suitable for long-term in vivo applications [3–5].

A current area of research in our laboratories is organosilicate nanocomposites. Nanocomposites are well represented in the literature and have been the focus of much interest since researchers discovered mechanical property trends that were unique in the field of composites [6,7]. Nanocomposites have been explored predominantly for industrial application, with few studies aiming to exploit the enhancement of mechanical and barrier properties for application in biomaterials. However, increasingly of late, studies have explored the potential of silicates to modulate drug release from hydrogels (e.g. [8,9]).

In the present study, we explore the hypothesized potential of layered silicates in a PEU matrix to mitigate in vivo degradation. Organosilicate nanocomposites have not been assessed in the published literature for in vivo biostability as far as we are aware. Our hypothesis was based on the fact that one layer of montmorillonite (MMT), a commonly used silicate, is 250 nm in two dimensions and 1 nm in the other, giving an aspect ratio of 250 and total surface area of over 700 $m^2 g^{-1}$ [10]. Layers naturally stack in groups on the order of 1000 units, but these can be at least partially delaminated by exploiting the cationic exchange capacity (CEC) of the layered silicate to organically modify the inorganic silicate and increase its compatibility with the organic polymer matrix. It is now well accepted that the dispersed high surface area particles confer barrier effect properties to the polymer. Accordingly, we hypothesized that the included partially delaminated silicate layers would act as a barrier to attack and ingress of degradation species in vivo, thus protecting ether linkages and inhibiting degradation.

2. Materials and methods

2.1. Poly(ether)urethane

PEU with chemical structure illustrated in Fig. 1 was used in this study. The polymer was supplied by Urethane Compounds (Melbourne, Australia) and contained ~65 wt.% 1000 g mol^{-1} poly(tetramethylene oxide) polyol ether soft segment, 4,4′-diphenylmethane diisocyanate and 1,4-butanediol as the chain extender. The components were combined in the molar ratio 100:7.5:46.3, respectively,

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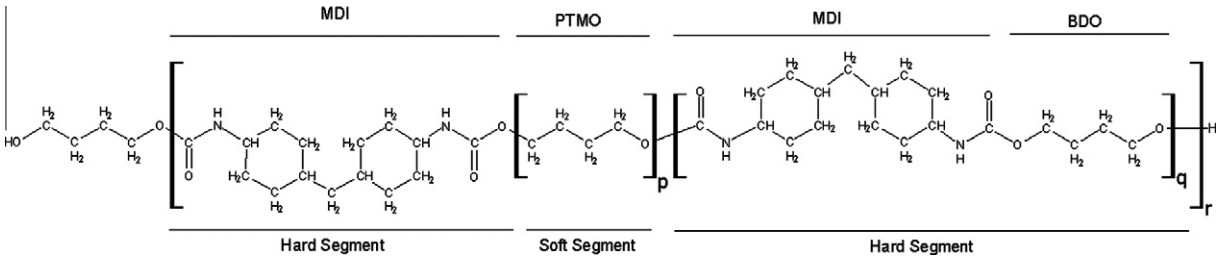

Fig. 1. Molecular structure of PEU.

with 0.003 dibutyltin dilaurate added as a catalyst. This is modelled on Pellethane® 2363-80A.

2.2. Layered silicates

A commercially available organically modified MMT, Cloisite® 30B (QACMMT; Southern Clay Products), was used. QACMMT had the quaternary ammonium compounds (QAC) methyl tallow bis-2-hydroxyethyl ammonium chloride as an organic modifier. This QAC is derived from animal adipose tissue, with the tallow indicating an alkyl chain of varying carbon atoms in length: 5% C_{14}, 30% C_{16} and 65% C_{18}. As a control, MMT ($Na_{0.33}[(Al_{1.67}Mg_{0.33})Si_4O_{10}(OH)_2]\cdot H_2O$; Southern Clay Products), of CEC 92.6 m Eq/100 g, was organically modified with amino undecanoic acid (AUA; Aldrich) by a method described previously [11]. The organically modified MMT thus prepared was referred to as AUAMMT.

2.3. Composite preparation

Composites were prepared from PEU and either (i) QACMMT or (ii) AUAMMT by a solvent casting method. Composites with loadings ranging from ~1 to 15 g nanoparticle/100 g PEU (1–15 wt.%) were prepared as detailed in Table 1. For details of the preparation methods and characterization of the resultant material, the reader is referred to our previous publication [11].

2.4. Composite biostability evaluation

2.4.1. In vivo ovine model

Methods were based on those published previously [3–5]. Briefly, dumb-bells were punch-cut from composite materials and strained to 150% over polymethylmethacrylate (PMMA) holders. The holders were engraved and tracked by a random code that was not broken until completion of the analysis. Strained samples were washed for 30 min in 2% Decon90 with manual agitation, rinsed at least six times in Milli-Q water, subjected to EtO sterilization and then degassed at room temperature for at least 7 days. All samples were taken from a single material batch, with the number of samples tested detailed in the following sections.

Ethics approval was granted by the Animal Care and Ethics Committee at The University of New South Wales (ACE #03/81). Samples were implanted subcutaneously in the dorsal region of sheep (healthy crossbred males, weighing 40–60 kg and ~2 years of age) for a time period of 6 weeks. Replicate samples were implanted into each of four sheep. One sample was assigned for histological analysis and another randomly selected post-assay for Fourier transform infrared (FTIR) analysis, while four samples were reserved for scanning electron microscopy (SEM) imaging and rating. Unimplanted control samples were also prepared (three per material) for FTIR and SEM analysis. Explanted samples were washed in 0.1 M NaOH for 5 days to remove attached biological tissue and proteins, rinsed in Milli-Q water, washed in 2% Decon-90 for 3 days to remove fatty deposits, rinsed again with Milli-Q water for 4 h and finally dried in a laminar flow hood. Unimplanted control samples were washed by the same process for consistency. Samples remained strained on the PMMA holders during both FTIR and SEM analysis.

Table 1
Material loadings for PEU, PEU-QACMMT and PEU-AUAMMT materials.

Material	Loading (g/100 g PEU)		
	Nanoparticle	Silicate	OM
PEU	0	0	0
PEU-QACMMT-1	1.0	0.8	0.2
PEU-QACMMT-3	3.0	2.4	0.6
PEU-QACMMT-15	15.0	12.1	2.9
PEU-AUAMMT-1	0.9	0.8	0.1

2.4.2. Scanning electron microscopy

Samples were coated with a ~20–30 μm thick layer of conductive gold using a Dynavac SC150 sputter coater and analysed using a Cambridge Stereoscan 360 SEM operated at an accelerating voltage (extrahigh tension) of 20 kV, with a typical working distance of ~20–27 mm. The system for objectively rating degradation employed was developed by Martin et al. [4]. SEM images from five set locations along the neck region of each sample were collected at ×50, ×150, and ×500 magnification per location, for each of four replicate samples, taken one per sheep. One image at ×10

Table 2
Biostability-relevant infrared absorption wave numbers.

Wavenumber (cm^{-1})		Description of proposed peak assignment
Literature	Experimental [a]	
1038	1038[b]	Stretching of the Si–O–Si bonds in MMT
1081	1075 ± 9.49	Aliphatic symmetric stretching of the hard segment ether C–O–C
1100	1099 ± 1.31	Aliphatic asymmetric stretching of the soft-segment ether C–O–C
1174	1176 ± 0.17	Bending of branched ether C–O–C degradation product
1208	1208[b]	Twisting of CH_2
1219	1220 ± 0.77	Stretching of C–N
1251	1251 ± 0.24	Wagging of CH_2
1365	1367 ± 0.16	Bending of CH_2
1446	1446[b]	Bending of CH_2
1529	1530 ± 0.69	Stretching of C–N and bending of N–H
1597	1597 ± 0.60	Stretching of C=C in aromatic ring
1703	1699 ± 0.57	Stretching of hard segment C=O hydrogen bonded to amine
1730	1728 ± 0.43	Stretching of non-hydrogen bonded hard segment C=O
2797	2795 ± 0.41	Symmetric stretching of C–H in $–CH_2O–$
2852	2852 ± 0.36	Asymmetric stretching of CH_2CH
2922	2919[b]	Dichroic parallel stretching of CH_2
2938	2938 ± 0.88	Asymmetric stretching of CH_2
3305	3322 ± 0.79	Stretching of N–H hydrogen bonded to carbonyl

[a] Average of all materials (unimplanted and implanted), not correcting for the Si–O–Si peak.
[b] Experimental peak not well defined, so the theoretical peak location was taken.

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