Thermoplastic Polyurethane (TPU) / Organo-fluoromica Nanocomposites for Biomedical Applications: In Vitro Fatigue Properties

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Abstract. Poly(dimethylsiloxane) (PDMS) / poly(hexamethylene oxide) (PHMO)-based thermoplastic polyurethane (TPU) nanocomposite was investigated for potential use in biomedical application. Studies on the in vitro fatigue behaviour of the TPU and TPU nanocomposite (under physiological saline solution, 37°C conditions) were highlighted in this article. The data were compared with those of commercially available silicone elastomer (Nusil MED 4860). Results indicated that the TPU nanocomposite (2MED-C (2HM)) had greater fatigue properties than the virgin TPU, which provide strong evidence of its greater capacity to withstand cyclic forces than the host TPU when exposed to physiological fluid. This was caused by the presence of well dispersed and impermeable organofluoromica platelets in the TPU matrix resulted in more tortuous path for the physiological fluid diffusion, thereby decreasing the fluid permeability of the polymer. Eventhough the silicone elastomer has lesser hysteresis than the virgin TPU and TPU nanocomposite, its fatigue strength is much lower than those of the TPU nanocomposite. The findings revealed the potential of PDMS/PHMO based TPU nanocomposite to replace silicone elastomer as biomaterial, particularly for implantable biomedical device application.

1 Introduction

Thermoplastic polyurethanes (TPUs) are linear, segmented block copolymers consisting of hard and soft segments. The hard segments are made from diisocyanate and short chain extender molecules such as diols or diamines, are rigid and highly polar. Hard segments have high inter-chain interaction due to hydrogen bonding between the urethane/urea groups [1]. The hydrogen bonding associations within the hard segments of the TPUs act as reinforcing filler for the soft matrix. On the other hand, soft segments consist of long, linear

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flexible polyether or polyester chains which interconnect two hard segments. In brief, the hard segments act as multifunctional tie points working as both physical crosslinks and reinforcing fillers, while the soft segments primarily influence the elastic properties of TPU [1, 2]. Thermoplastic polyurethanes (TPUs) are promising candidates for use as biomaterials in the fabrication of a wide range of medical devices due to the relative ease of fabrication, flexibility, good blood contacting properties, biostability and excellent insulation properties [3, 4]. The poly(dimethylsiloxane)(PDMS)/poly(hexamethylene oxide)(PHMO)-based TPU based on an optimized formulation (Elast-Eon™) from AorTech International Pty Ltd exhibits physical properties comparable to those of medical grade polyether-based TPU materials such as Pellethane™ 80A and is now widely accepted as being amongst the most biostable of all the commercial TPUs [5]. Our previous work demonstrates that the Elast-Eon E5-325 TPU can be tailored to provide advantageous mechanical properties by incorporating organically modified smectic nanosilicates [6-8]. We found that the best surface modification was obtained with the most hydrophobic / dual surfactants system (namely the 75% dimethyldioctadecylammonium chloride (DODMAC) & 25% Choline chloride) [6, 7]. The TPU nanocomposite with organofluoromica (fluoromica surface modified with DODMAC/CC) was then selected for further evaluation on the biostability aspects. To safely utilize these PDMS/PHMO-based TPU nanocomposites in human biological systems, assessing the mechanical performance under specific conditions and environmental influences is also essential, given that the TPU nanocomposite is to be exposed in the human physiological fluid. In vitro tests in liquid media closely mimicking physiological chemical conditions and temperature, are essential for “screening” this TPU nanocomposite for eventual use in implantable devices, and prior to committing to expensive in vivo tests in appropriate animal models. For this work in particular, it is of great importance to assess the time-dependant dynamic mechanical integrity by employing fatigue test. Fatigue is a failure mechanism which occurs when the material is subjected to a cyclic load or repeat stress [9].

In this communication, the in vitro mechanical properties of the PDMS/PHMO TPU nanocomposites incorporating organofluoromica were reported and compared to those of the commercial silicone elastomer (Nusil MED 4860). The samples have been subjected to in vitro condition by immersing the host TPU and nanocomposite samples in physiological saline solution at 37°C. The in vitro fatigue test was carried out to predict the potential improvements in long-term in vivo performance of the TPU nanocomposites for implant applications.

2 Materials and Methods

2.1 Materials

Thermoplastic polyurethane (TPU) was supplied by AorTech Biometers Pty Ltd (VIC, Australia). This TPU is commercially known as ElastEon™E5-325 TPU consists of a 1000 g/mol poly(dimethylsiloxane) (PDMS) and 700 g/mol poly(hexamethylene oxide) (PHMO) mixed soft segment in a 98:2 (w/w) ratio, and a hard segment composed of alternating 4,4’-methylene diphenyl diisocyanate (MDI) and 1,4 butanediol (BDO) sequences. The hard segment concentrations is 32.5 wt%. Nusil MED 4860 is a medical grade elastomer with a two-part silicone system in 1:1 mix ratio (Part A:B). Part A consists of 30wt% amorphous silica, while part B is a 5 wt % dimethyl, methylhydrogen siloxane copolymer. When these two components are mixed, Nusil MED 4860 undergoes rapid 5 min curing at 165 °C due to the presence of a platinum catalyst. This material was supplied by CochlearTM Ltd and is commercially available from Nusil (via EIM Medical Consulting Pty Ltd, NSW, Australia).
Somasif ME100 (ME) a synthetic fluoromica (tetrasilicic trioctahedral fluoromica) was supplied by Kobo Products, Inc (N.J., USA). It is a fine white powder with an average platelet length of approximately 650 nm. This fluoromica was surface modified with dual modification system (75% dimethyldioctadecylammonium chloride (DODMAC) & 25% Choline chloride) to obtain the ‘hydrophobic organo-fluoromica’ as nanofiller for this study. This dual surface modified fluoromica (organo-fluoromica) was chosen in this study because it has previously resulted in the best mechanical performance when incorporated into the TPU due to its hydrophobic characteristic that can provide more favourable TPU-nanofiller interactions.

2.2 Methods

**High Energy Milling Process for Organo-fluoromica (MED-C)**

High energy milling on the organo-fluoromica was done using a Netzsch Laboratory Mill type LABSTAR LS1. The 0.4 mm Yttrium-stabilized zirconium oxide (ZrO2) grinding beads were employed as milling media. The milling was done in an ethanol/water mixture at a 1:1 ratio. The organo-silicate was milled for 2 hours to reduce its particle size from ~650nm to ~250nm. The milled MED-C suspensions were then separated by centrifugation using a Beckman Coulter Allegra X-15 benchtop centrifuge with a rotation speed of 4750 rpm for 3 min, and subsequently washed with MilliQ water (18.2 MΩ.cm). The washed clay was dried in an oven at 60 ºC overnight and ground by jet milling prior to nanocomposite processing.

**Preparation of the TPU Nanocomposite Sheets**

E5-325 TPU was used as matrix material in this study. The two hour milled organofluoromica (MED-C (2HM) were used as nanofillers. E5-325 TPU nanocomposite containing MED-C (2HM) was prepared with a 2 wt% nanofiller composition by using melt processing (MP) method. In the subsequent discussion, these nanocomposites are referred to as 2MED-C (2HM). A number denotes the 2 wt% organosilicate loading in the TPU. The first two letters represent the nanosilicate used (ME=Somasif ME100) and the last two letters (D-C) represent the dual DODMAC/CC surface modification. The characters in the brackets; (2HM) denote the nanofiller size reduction process of 2 hour high energy milling. E5-325 TPU nanocomposites were prepared by melt compounding the TPU pellets with 2 wt% organo-fluoromica using a Haake Rheomex OS twin screw extruder (Thermo Scientific, USA). The extrudate was pelletized and dried at ~70 ºC for approximately 20 hours prior to being compression moulded. Compression moulding was performed using a hydraulic press. A pair of brass plates was used, with the bottom plate having a rectangular cavity. The moulds were heated to 185 ºC, prior to the pellets being added. A “pre-press” was done at 1 kPa for 1 minute, followed by 5 kPa for 0.5 minutes. Pressure was released to remove any further air bubbles then the samples were pressed for a further 0.5 minutes at 7.5 kPa. The samples were cooled under pressure to about 140 ºC using a controlled water flow without releasing pressure. Approximately 1mm thick plaques were produced and they were then annealed under vacuum at 85 ºC for approximately 5 hours and left for at least a week to age prior to testing.

**In vitro fatigue test**

In order to obtain sensible in vitro results, the test was performed in an environmental chamber containing phosphate buffered saline (PBS) solution (Ph ~7.4). In addition, 0.02% sodium azide was added to the solution to retard the microorganism growth, and the test was performed at 37ºC condition, which approximates human body temperature. The test samples were conditioned for at least 30 minutes in the environmental chamber before proceeding to the mechanical test. Dumbbell samples which were punched from an ASTM D-638-M-3 die
were employed for each test. A cyclic tensile load of 500 N was applied axially at 0.2 Hz for 10,000 cycles. Cyclic strain amplitude of 50 % was applied, and the test was recorded using a sinusoidal waveform and a 50 ms data acquisition rate. Hysteresis was calculated on the 5th cycle to 125 % using the equation below [10]:

\[
\text{Hysteresis} \, (\%) = \frac{\text{Area bound by the loading and unloading curve}}{\text{Area under the loading curve}} \times 100
\]  

(1)

Transmission Electron Microscopy (TEM) Analysis

TEM analysis was done to observe the dispersion of organofluoromica platelets throughout the TPU matrix. Thin sections of approximately 80 nm thickness were cut using a Diatome diamond knife on a Leica Ultracut UC6FCS cryogenic ultramicrotome between -80 and -110°C to ensure the polymers were rigid. Sections were picked up using a loop of 2.3M sucrose and mounted on 200 mesh copper grids (ProSciTech, Australia). Grids were placed on droplets of deionized water and then transferred through five washes. The grids were then allowed to air dry in self-closing forceps prior to viewing. Sample was examined at high magnification (93000×) on a Technai F30 FEG TEM (FEI company, Netherlands) operating at 300 kV and images were captured with a Direct Electron LC1100 Lens-Coupled 4k × 4k CCD camera system.

3 Results and Discussion

In vitro (in PBS, 37°C) fatigue properties of silicone elastomer (MED 4860), virgin TPU and TPU nanocomposite

In this work, fatigue test was carried out to determine the behavior of materials in physiological fluid, 37°C under fluctuating loads. Since long term stability in vivo is critical for biomedical use, changes in deformation and properties due to fatigue behaviour should also be addressed. It has been discovered that the TPU consists of an elastic portion which stores energy and returns it, and a viscous portion which captures energy and converts it to heat [11, 12]. At 37°C, soft segments are above their glass transition temperature and impart the material its elastic behavior, while hard segments are below their glassy or melt transition temperature and are thought to govern the plastic deformation, high modulus, and tensile strength [11, 12]. This unique TPU morphology evolves with deformation and this evolution is thought to be the primary source of hysteresis and cyclic softening [11-13]. Hysteresis is a measure of absorbed or dissipated energy during any cycle of loading or unloading when material is subjected to repeated loading [11, 12]. Most TPU show hysteresis characteristic, and this can be attributed to a number of factors such as non-affine deformation, irreversible orientation of the hard domains, plastic deformation of the hard domains and energy losses caused by the hard domain orientation [12]. The breakdown and reformation of the TPU mesophase morphology during the cyclic loading are responsible for the stress-softening (Mullin effect) and hysteresis losses. This may somehow contribute to a reduction in mechanical integrity [12, 14]. The area between the two curves is the energy which is not returned but is converted to heat. The hysteresis loop may yield information on fatigue degree [14]. The modification of hysteresis loop with cycle is associated with the stress variation with time, which is depends on the cyclic stability of the tested material. Large modification in hysteresis loop upon high cyclic loading is the indication of cyclic softening or reduction in mechanical strength [14]. For comparison on the cyclic effect, the hysteresis loops from the cycle number of 5, 100, 1000 and 10,000 were obtained from the stress-strain curves during the fatigue test and they are presented in Figure 1.
Fig. 1. Hysteresis loops of Nusil MED 4860, E5-325 and 2MED-C (2HM) taken at cycle number a) 5 b) 100 c) 1000 d) 10000

Table 1: *In vitro* fatigue properties of Nusil MED 4860, E5-325 TPU and 2MED-C (2HM)

| Number of cycles | Hysteresis loop area (MPa) |
|------------------|---------------------------|
|                  | Nusil MED 4860 | E5-325 | 2MED-C (2HM) |
| 1                | 4.533606       | 11.87614 | 18.95885 |
| 5                | 2.773143       | 8.884384  | 14.27935 |
| 10               | 2.530383       | 8.11088   | 13.11338 |
| 100              | 2.102186       | 6.123003  | 9.957682 |
| 1000             | 1.656158       | 5.051902  | 8.130133 |
| 10000            | 0.877921       | 4.269729  | 6.851635 |

Differences in loop area between the 1st cycle and 10,000th cycle: 81%, 64%, 64%
Silicone elastomer generally has lesser hysteresis than TPU due to the absence of structure contributing to plastic deformation and stress relaxation. This can be clearly observed in the Nusil MED 4860, which demonstrate much lower hysteresis than the E5-325 TPU (virgin and nanocomposite). As can be seen from Table 1 and Figure 1, the hysteresis loop of 2MED-C (2HM) shows a larger area than the virgin TPU (E5-325), indicating greater energy dissipation, which is mainly due to the friction of the nanofiller surface and the TPU chains [12]. It is well established that the incorporation of fillers to elastomers causes an increase in hysteresis [11, 14, 15]. Of particular interest, the addition of the organofluoromica into the TPU only resulted in 5% increase of hysteresis. However, the percentages of reduction in the hysteresis loop area after 10,000th cycle are the same for both E5-325 TPU and 2MED-C (2HM) nanocomposite (see Table 1). This suggests that the incorporation of organofluoromica did not increase the fatigue degree at high cyclic loading (10,000th cycles). Furthermore, 2MED-C (2HM) nanocomposite also performs the highest fatigue strength by demonstrating the highest maximum stress values, both in low and high cycles. For instance, the fatigue strength of 2MED-C (2HM) measured at 10,000th cycle exhibits an increase by 40% with respect to the virgin TPU. Several findings concluded that dynamic stresses promote chain scission, crack initiation and propagation in other synthetic elastomeric materials when tested under environmental challenged conditions [9, 11, 16]. However, the incorporation of well dispersed nanofiller might retard these processes [13]. As shown in TEM image in Figure 2, 2MED-C (2HM) nanocomposite demonstrates the dispersive and distributive mixing system. Upon deformation, the well dispersed and exfoliated organofluoromica (MED-C (2HM)) platelets might act as nano-barriers for crack propagation, and hence leading to an increase of fatigue resistance. This nano-barrier effect has been explained by Jin et al. [13] who hypothesized that, the incorporation of the organomontmorillonite in the TPU resulted in an increase in fatigue strength due to the formation of ‘nanospring-like’ system composed of two nanoplatelets and polymer chains, which are intercalated in the two nanoplatelets. Upon cyclic loading, these ‘nanospring-like’ systems undergo reversible deformation, thereby capable of absorbing deformation energy and preventing the development of fatigue cracks. It is also worth mentioning that when the TPU being immersed in the PBS solution, the permeant (physiological fluid) can result in weakening of hydrogen-bonded hard segment domains and secondary bonding between the TPU chains. However, TEM image in Figure 2 reveals good dispersion of organofluoromica in the structure of 2MED-C (2HM) nanocomposite. This reduce the permeability of the physiological fluid inside the MED-C (2HM) nanocomposite structure due the tortuosity effect, induced by the well dispersed and exfoliated organofluoromica platelets. As a result, the fatigue strength of the 2MED-C (2HM) nanocomposite was superior to the virgin TPU when exposed to PBS solution, 37°C.
4 Conclusion

Our preliminary studies on the \textit{in vitro} fatigue show promising properties of the E5-325 TPU nanocomposite (2MED-C (2HM)), which possess the potential to be further developed for biomaterials. When subjected to the \textit{in vitro} conditions, 2MED-C (2HM) shows the highest fatigue strength by obtaining the highest maximum stress values, both in low and high cyclic loading (up to 10,000 cycles). The well dispersed and exfoliated organofluoromica platelets might act as nano-barriers leading to an increase of fatigue resistance. The data reported here are evidence that well-engineered nanofiller systems may assist the TPU performance under the environmental challenge environment. If carefully formulated, this nanofiller can bring positive influence on the viscoelastic properties such as creep and fatigue, in addition to ultimate tensile strength and tear strength. Although, the preliminary \textit{in vitro} fatigue test was performed as more of a proof-of-concept stage, the results gained from this study should provide a useful measure of predicting the E5-325 TPU nanocomposite biostability, essential for the development and design of future biomedical TPU nanocomposites. Thus, these findings may merit further investigation on long-term \textit{in vitro} and \textit{in vivo} mechanical properties and stability under varied environmental ageing for complete investigation on the biostability and biocompatibility of this nanocomposite system.

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