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Composite hydrogels for intervertebral disc prostheses

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Different PHEMA/PCL semi-IPNs hydrogels and their relative composite systems reinforced with PET fibres have been investigated for potential use as intervertebral disc prostheses. Compression properties and water absorption were evaluated. Uniaxial compression tests on the swollen samples showed an increase of the modulus and maximum stress with increasing content of PCL and PET fibres. In particular, the composite PHEMA/PCL hydrogels showed compression properties similar to those expressed by the canine intervertebral discs in different spinal locations. The equilibrium water content of modified semi-IPNs decreased as function of the PCL and PET fibres. These tests indicate that the use of composite hydrogels as disc prostheses is very promising because it is possible to combine transport and mechanical properties which are crucial for the performance of the intervertebral disc.

1. Introduction

The intervertebral disc is a fibrocartilaginous complex that forms the articulation between the bodies of the vertebrae. The discs of the various spinal regions may differ considerably in size and in some detail, but they are basically identical in their structural organization. Each consists of two components: the internal semi-fluid mass, the nucleus pulposes, and its laminar fibrous container, the annulus fibrous. Both are anchored to the vertebral bodies by cartilaginous end-plates.

The nucleus pulpous occupies an eccentric position within the confines of the annulus, usually being closer to the posterior margin of the disc. The annulus is a concentric series of fibrous lamellae that encase the nucleus and strongly unite the intervertebral bodies. Whereas the essential function of the nucleus is to resist and redistribute compressive forces within the spine, one of the major functions of the annulus is to withstand tension, whether the tensile forces be from the horizontal extension of the compressed nucleus, from the torsional stress of the column or from the separation of the vertebral bodies on the convex side of spinal flexure.

The composition of the intervertebral disc is very similar to that of articular cartilage. It consists principally of collagen fibres embedded in a proteoglycan–water gel. The latter component develops a large swelling pressure which enable the disc to resist compressive properties [1].

The type and orientation of collagen in the disc have an important influence on how load is distributed. In the disc there is a gradation of collagen type and orientation from nucleus to annulus. The collagen fibres contained in the concentric lamellae are inclined with respect to the vertical axis of the spine in a lay-up structure. From the edge of the disc inwards to the nucleus, the angle of fibre orientation decreases from 62 to 45 degrees [2]. Water is the main constituent of the disc, it occupies 65 to 85% of the tissue volume, depending on age and region.

Contained within the matrix are cells which actively maintain and repair it. The transport properties of the disc are very important since they control the nutrition and the mechanical properties [1].

The pathology of the intervertebral disc is mainly related to ageing and insufficient nutrition; in fact, with age the nucleus loses its gel-like character, compressive stress are then no longer evenly distributed to the end-plates and annulus. High concentration of stresses in the annulus may occur and lead to degeneration. More critical situations due to injuries such as complete rupture of a disc could be solved by using artificial discs. The current available intervertebral disc prostheses are made of metals, metallic-polymer systems and polymers [3–6]. Unfortunately, their performance is not yet acceptable for long-term applications.

In order to reproduce the unique mechanical and transport properties of intervertebral disc, a composite hydrogel structure is proposed.

Hydrogels are polymeric networks held together by covalent bonds and weaker cohesive forces such as

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hydrogen or ionic bonds. These networks are able to retain a large quantity of water within their structure, without dissolving. Hydrogels include many natural materials of both plant and animal origin; as a result of this, they have been used in a wide variety of biomedical applications. Attributes such as permeability to small molecules (such as tissue metabolites) and their soft consistency are important properties that makes them attractive as the matrix for composites for soft tissue prostheses [7, 8].

Due to their biocompatible characteristics, high permeability and high hydrophilicity, poly(2-hydroxyethylmethacrylate) (PHEMA) hydrogels have potential use as the matrix of an artificial disc. However, the mechanical properties of these materials in the hydrated state are inadequate for biomedical applications where mechanical strength is required.

Previous works [9, 10] has shown that the incorporation of hydrophobic component such as poly(caprolactone) (PCL) into PHEMA hydrogels results in materials exhibiting improved mechanical properties. In this paper the compression properties of PHEMA-PCL semi-interpenetrating networks (s-IPNs) and PHEMA-PCL s-IPNs reinforced with PET fibres are investigated and compared with those found in canine intervertebral disc [11].

2. Materials and methods

2.1. Preparation of PHEMA/PCL Semi-IPN Hydrogels

Polycaprolactone (MW = 35.000), was dissolved in 2-hydroxyethylmethacrylate (HEMA) monomer at 60 °C. After allowing the solution to cool, 0.5 wt % EDMA crosslinking agent on 0.1 w % AIBN initiator were added. The percentage of initiator and crosslinking agent were calculated with respect to HEMA. The mixed solution was poured into a cylindrical mould of inner diameter 10 mm, and cured at 90 °C for 1 h. After cooling, each sample was placed in distilled water at 37 °C until water absorption equilibrium was reached, then 15 mm length rods were obtained for compression testing. The semi-IPNs prepared covered the compositions 10% (b), 20% (c), 30% (d) by weight of PCL in PHEMA.

PHEMA samples (a) were prepared by adding 0.5 wt % EDMA crosslinking agent and 0.1 wt % AIBN initiator to HEMA monomer and then using the semi-IPNs sample preparation procedure.

2.2. Preparation of PHEMA/PCL semi-IPN composite hydrogels

Polyethylenetherephtalate (PET) continuous fibres (kindly supplied by Montefibre S.p.A.) were wound helically by filament winding machine on polyethylene hoses with diameters of 6 mm. The fibres were preimpregnated in the reactive solutions described previously and wound on the hose mandrel until a final diameter of 10 mm was reached. The winding angle was varied, from inside to outside, from 45 to 65 degrees and from 45 to 90 degrees. The impregnated wound fibres were carefully removed from the mandrel and placed into a cylindrical mould having an inner diameter of 10 mm. The reactive solution was then poured in the mould and cured at 90 °C for 1 h. After cooling the samples were placed in distilled water for hydradation, then rods of 15 mm length were used for testing. This technique permits preparation of samples with a softer and more hydrophylic inner part (i.e. nucleus) and a harder and less hydrophilic outer part (i.e. annulus).

2.3. Water absorption

Disc-shaped samples of each hydrogel and composite structure were dried in the oven at 50 °C under vacuum for 48 h, then weighed and exposed to distilled water in a water bath at $T = 37$ °C. Samples were weighed periodically to determine the equilibrium amount of water absorbed. This quantity was calculated as the difference in the sample weight of swollen polymer and weight of dry polymer, divided by the weight of swollen polymer.

2.4. Compression test

Five samples of each composition and composite structure were tested in compression in the form of cylinders of length 15 mm and diameter approximately 12 mm according to the water content. The compression tests were performed by screw-driven Instron 4204 mechanical testing machine. Specimens were placed between stainless steel plates, immersed in distilled water at $T = 37$ °C, and compressed at a rate of 10 mm/min.

3. Results and discussion

The aim of this study was to design a novel composite intervertebral disc prostheses by using hydrogel systems in order to obtain transport and mechanical properties similar to those of the natural systems. Several disc prostheses are available but none of them take into consideration the hydrophilic characteristics and hence the real properties of the natural disc.

Our design approach is based on the necessity of reproducing such features; hydrophilic composite structure were hence prepared and their mechanical properties were compared to those obtained from canine intervertebral discs [11].

Several hydrophilic semi-interpenetrating polymeric networks were prepared by inclusion of the hydrophobic poly-caprolactone in poly(2-hydroxyethylmethacrylate) to improve the mechanical properties. Since swollen PHEMA hydrogel is a weak elastomeric material, the incorporation of the hydrophobic component, which remains unaffected by water, will reinforce the mechanical properties of PHEMA hydrogels [10].

The stress–strain curves in compression of swollen semi-IPNs are reported in Fig. 1. It can be observed that the compression properties are improved as the concentration of PCL increases in the semi-IPNs. The values of the elastic modulus and maximum stress and strain of semi IPNs are reported in Table I. The increase of elastic modulus and maximum stress is due

TABLE I Compressive properties of swollen PHEMA/PCL semi-IPN

Sample	E (MPa)	σ_{max} (MPa)	ε_{max} (mm/mm)
PHEMA (a)	1.02 ± 0.06	0.51 ± 0.02	0.51 ± 0.03
PHEMA/PCL 90/10 (b)	2.10 ± 0.16	1.45 ± 0.08	0.55 ± 0.02
PHEMA/PCL 80/20 (c)	6.21 ± 0.14	2.48 ± 0.06	0.44 ± 0.01
PHEMA/PCL 70/30 (d)	15.95 ± 1.07	7.27 ± 0.06	0.54 ± 0.02

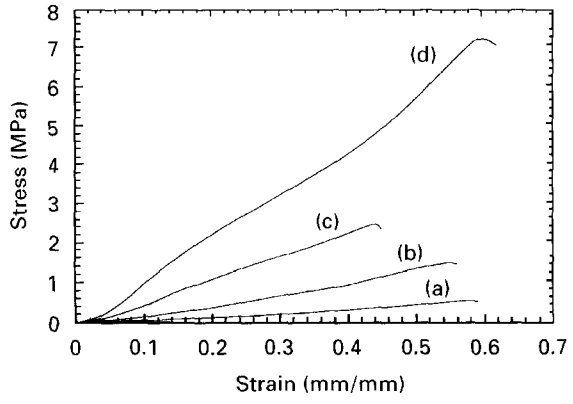

Figure 1 Stress–strain curves in compression of swollen of PHEMA (a) and PHEMA/PCL 90/10 (b), PHEMA/PCL 80/20 (c), PHEMA/PCL 70/30 (d) semi-IPNs.

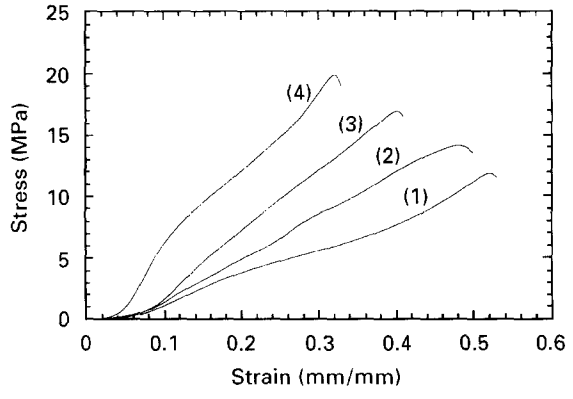

Figure 2 Stress–strain curves in compression of swollen composite semi-IPNs reinforced with 40% by volume PET fibres having winding angle from 45 to 65 degrees (1), (2), (3) and PHEMA/PCL 70/30 reinforced with 50% by volume PET fibres having winding angle from 45 to 90 degrees (4).

TABLE II Compressive properties of swollen composite PHEMA/PCL semi-IPNs reinforced with 40% by volume of PET fibres having winding angle from 45 to 65 degrees (samples 1, 2, 3) and composite PHEMA/PCL 70/30 semi-IPN reinforced with 50% by volume of PET fibres having winding angle from 45 to 90 degrees

	E (MPa)	σ_{max} (MPa)	ε_{max} (mm/mm)
Sample (1)	30.17 ± 2.95	12 ± 0.6	0.52 ± 0.02
Sample (2)	60.82 ± 4.82	14.3 ± 0.39	0.48 ± 0.03
Sample (3)	73.3 ± 6.30	17.2 ± 1.25	0.40 ± 0.01
Sample (4)	129.7 ± 6.80	20.3 ± 0.9	0.32 ± 0.02

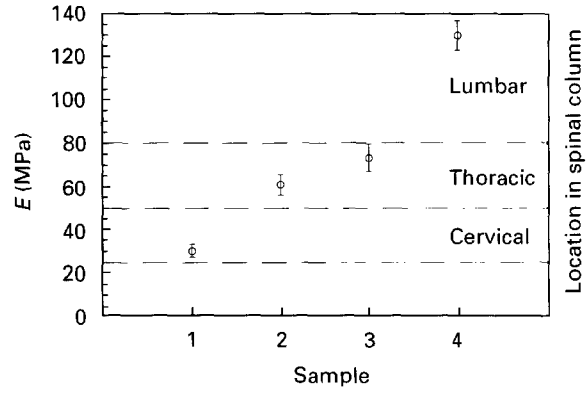

Figure 3 Compressive modulus of swollen composite semi-IPNs samples plotted against the compressive modulus value range of the canine intervertebral disc in different locations of the spinal column.

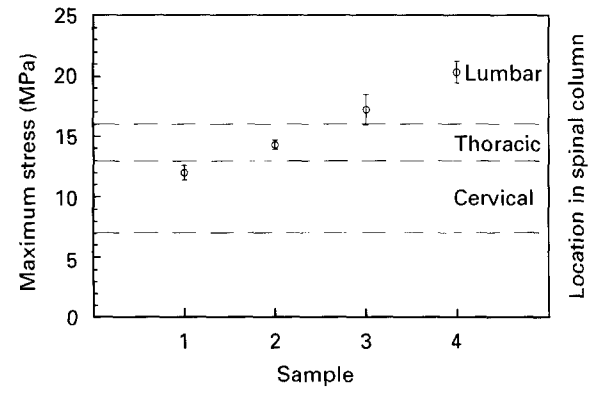

Figure 4 Compressive maximum stress of swollen composite semi-IPNs samples plotted against the compressive maximum stress value range of the canine intervertebral disc in different location of spinal column.

to the presence of PCL crystalline microdomains which act as physical crosslinks, contributing to an increase in the compression properties of the modified hydrogels.

The values of modulus and maximum stress of the canine discs vary, respectively, from 32 to 115 MPa and from 8 to 19 MPa, as a function of the spine location [11], and these values are significantly higher than those obtained from semi-IPNs themselves. To improve the compression properties of the modified hydrogels a composite structure was obtained by reinforcing the semi-IPNs (sample b, c, and d) with about 40% by volume of PET fibres with winding angles varying from 45 to 65 degrees (respectively named: sample 1, sample 2 and sample 3).

The stress–strain curves in compression of swollen composite systems are presented in Fig. 2. An initial toe region followed by a linear region can be observed, and this trend is qualitatively similar to that of the natural disc [11]. As reported in Table II, an increase of elastic modulus and maximum stress was observed, while a decrease of maximum strain was obtained. The value of the modulus increased from 30 to 73 MPa and the maximum stress from 12 to 17 MPa. Considering the respective values of canine disc it can be observed that the composite semi-IPNs (samples 1, 2 and 3) presented optimum compressive properties for intervertebral disc in the cervical and thoracic region, as shown in Figs. 3 and 4.

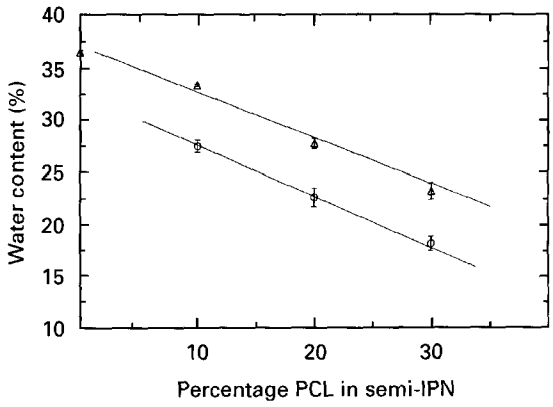

Figure 5 Equilibrium water content of PHEMA/PCL semi-IPNs (△) and composite PHEMA/PCL semi-IPNs reinforced with 40% by volume of PET fibres (○).

Since the values of the modulus and stress of canine intervertebral disc in the lumbar region are higher, a different composite structure is proposed. PHEMA/PCL 70/30 was reinforced with 50% by volume of PET fibres with winding angle varying from 45 to 65 degrees; at the end a 90° winding angle was used (sample 4). The stress–strain curve in compression is represented by the curve (4) and related properties are reported in Table II. As expected, the increase of PET content and the presence of fibres at 90° at the end of the periphery resulted in an increase in the modulus in the linear region, an increase of the maximum stress and a reduction of the maximum strain. The value of the modulus and maximum stress are, respectively, 129 and 20 MPa, which are typical values of canine intervertebral disc in the lumbar region as shown in Figs. 3 and 4.

Inclusion of PCL reduced the hydrophilicity of the systems, as shown by the upper curve of Fig. 5. The equilibrium water content of modified hydrogels decreased with increasing content of PCL in the network and the maximum water absorption was observed for PHEMA hydrogel. However, up to 30% of PCL, the equilibrium water content is about 23% which is close to that of collagen [12].

The lower curve is representative of the equilibrium water content of the semi-IPNs reinforced with 40% by volume of PET fibres. The inclusion of the fibres caused a reduction of water absorption of only 16–19% with respect to the semi-IPNs. This is due to the fact that the composite structure occupies about 50% of the entire volume.

4. Conclusion

The use of a composite structure permits systems to be obtained with compression properties close to that of canine intervertebral discs from different locations in the spinal column. By varying the composition of the hydrogel matrix, the winding angle and the quantity of PET fibres, it is possible to modulate the hydrophilicity and the mechanical properties of intervertebral disc prostheses. Moreover, the PHEMA-PCL semi IPNs may allow natural tissue in-growth since PCL degrades to leave voids in the network. In this way the implant can be anchored to the body.

The results obtained in this study lead not only to the design of canine intervertebral disc prostheses, but give good indications for the use of these systems in human applications. For this latter purpose, future work will be focused on the design of composite systems whose matrix is composed of hydrogels, such as poly(N-vinylpyrrolidone)-based polymers [13, 14], having more appropriate hydrophilicity and mechanical properties.

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