HEMA Based Copolimers as Future Materials in Intervertebral Disc Replacements

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Degenerative disc disease in the lumbar spine is marked by a dehydration of the intervertebral disc and loss of biomechanical function of the spinal unit. Since the current surgical procedures are ineffective in restoring natural biomechanical function back to the diseased disc, researchers have looked to replace the intervertebral disc. These designs are flawed in that they either don't restore natural movement back to the spinal unit, require surgeries that are highly invasive, or they further promote disc degeneration of adjacent spinal levels. Recently, researchers have sought to only replace the central portion of the disc called the nucleus pulpous. A potential nucleus replacement could mimic a healthy nucleus pulpous in restoring healthy biomechanical function to the spinal unit. A hydrogel, poly (vinyl alcohol) (PVA), has been investigated to serve as a nucleus replacement. However, semi crystalline PVA suffers dissolution under physiological conditions and for this reasons are tested others hydrogels (HEMA) which are biocompatible, maintain the liquid transport function, the shape and the size of intervertebral disc and are very good shock-absorbent.

Keywords: prosthesis, hydrogel, HEMA, intervertebral disc

The present polymeric prosthesis relates to a spinal nucleus implant to replace all or a portion of nucleus pulpous or entire intervertebral disc which has been removed from a spinal disc of a living vertebrate, e.g. a human. This spinal nucleus implant is formed of a gel which is capable of anisotropic swelling.

Spinal intervertebral disc is a cartilaginous tissue located between the endplates of adjacent vertebra. The spinal intervertebral disc acts as a flexible joint between the vertebra, allowing bending and twisting of the spine column. Damage to the spinal intervertebral disc can cause spinal dysfunction, crippling pain and short- or long-term disability. Because of the wide occurrence of this problem (5% annual incidence of back pain due to the spinal intervertebral disc is reported), the economic consequences are enormous. Some disc problems require a surgery. Typical current procedure is fusion of the adjacent vertebra using various techniques and devices. All currently available surgical procedures, such as removal of the nucleus or its part (laminectomy), or fusion of adjacent vertebra, compromise spinal function in one way or another [1].

The spinal intervertebral disc acts primarily as a weight-bearing and flexible joint. It enables mutual rotation, bending and translation of the adjacent vertebra, while bearing a considerable axial load. In addition, the spinal intervertebral disc attenuates vibrations and mechanical shocks and prevents their propagation through the skeletal system The load bearing capability and flexibility in selected directions is achieved by the combination of the annulus fibrous and nucleus pulpous. Annulus fibrous is a layered structure that is rigid in the radial direction but deformable in the axial direction and by torque. The axial load is born by nucleus pulpous that transforms it partly into an axial component that is contained by the annulus fibrous. The annulus fibrous is formed mainly by collagen fibrils organized in several layers. Each layer has its collagen fibrils wound at an angle, and subsequent layers have an alternate orientation [1]. The collagen organization closely resembles organization of fiber reinforcement as in composites used for pressure vessels or cords in tires. It guarantees maximum resistance to radial stress (or internal pressure) while allowing a deformation in torque and bending.

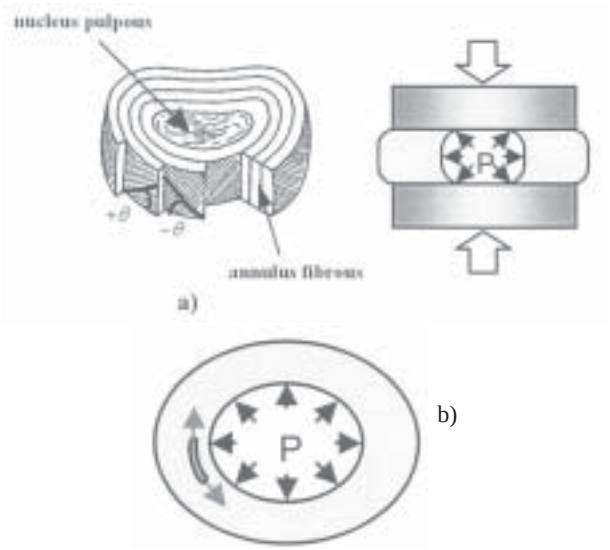

Fig..1 Mechanical behaviour of the intervertebral disc
a) anatomical structure; b) mechanical comportament

This structural complexity of spinal intervertebral disc is the consequence of complex requirements, not a whimsical excess of nature. Therefore, the disc replacement's function, properties and structure has to be a close approximation of the original disc in order to be able to perform all its functions. In other words, a successful disc replacement has to be biomimetic to the maximum degree achievable. This was not possible for a long time

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because there were no synthetic materials that could replicate structure, properties and functions of natural tissue. Because of that, most of the prostheses were designed as mechanical joints enabling certain movement of vertebra but not replicating all intervertebral disc properties.

The main problem of these devices is their limited functionality. Even more important, implantation of these devices is a very complex procedure requiring a major spine surgery with many associated risks, long-term recovery and high cost. There is an ongoing effort to develop better prosthesis of the disc that would more closely replicate its mechanical function. For instance, the "Functional and Biocompatible Intervertebral Spacer" (1990) describe a composite replacement of the disc made from a biocompatible elastomer reinforced with fibers that mimics the mechanical properties of the natural disc. It replicates the disc structure having an elastomeric core with the shape approximating the shape of nucleus pulpous, wrapped around by a fiber-reinforced elastomeric layers replicating structure of annulus fibrous. The reinforcing fibers have preferred orientation-simulating arrangement of collagen fibers in annulus fibrous. The faces of the assembly are equipped with tough elastomeric layers simulating the mechanical function of cartilaginous layers of vertebral endplates. This structure reasonably closely replicates the spinal intervertebral disc structure and its mechanical function. However, the implantation of this device is still very complex and costly, requiring a major spine surgery. In many cases, the pain relief requires that only nucleus pulpous (or even only its part) be removed rather than whole spinal intervertebral disc. In that case, the major part of the axial load is directly applied to annulus fibrous. Annulus fibrous is now stressed by the axial rather than radial load for which it is designed. Consequently, annulus fibrous delaminates, splits, fractures and brakes down gradually. The situation is somewhat akin to driving on a deflated tire. In this situation, it is useful to replace the missing nucleus pulpous (or its part) to reestablish the radial stress on annulus fibrous (or to "reinflate" the spinal intervertebral disc) that is required for its proper function. The nucleus pulpous replacement can be carried out by an easier, less traumatic and less expensive surgical procedure [1].

It is important to recognize that a successful replacement of nucleus pulpous has to replicate not only the mechanical function, but also the function of osmotic pump. Without that, the living tissue of vertebral endplate cartilages and annulus fibrous cannot be maintained in healthy condition. For those reasons, the nucleus pulpous cannot be replaced by a piece of a hydrophobic, non-hydrogel elastomer, such as silicone rubber or polyurethane.

Experiment part

Material and method

A biomaterial is a material designed to fulfil a purpose and to resist at a physiological interface without being rejected. A large number of biomaterials have been developed for the progressive use as biomedical devices, especially in recent years. One of the major growth areas in biomaterial research is the design and development of polymers to fulfill the growing number of biomedical requirements. The most important problem, when the using biomaterials is their biocompatibility [2, 3, 4, 6].

It is essential for an implanted device to be able to avoid physiological rejection at the biological interface to which it is applied. Rejection can be manifested in many ways depending on the biological environment of the implanted material. For example, a material rejected at a blood interface may cause thrombosis in a patient. A number of polymers are known and used as biomaterials which have a wide range of properties from hard and glassy plastics, through hydrophobic rubbery materials, to soft water containing hydrogels.

Polymer hydrogels based on copolymers of hydroxyethyl methacrylate (HEMA) and other methacrylate monomers have a range of potential applications in the medical fields. This hydrogel prosthesis need to maintain the liquid transport function and that has, in its fully hydrated state, the shape and size generally conforming to a missing natural nucleus. This hydrogel prosthesis relates to a biomimetic spinal nucleus implant designed to restore the function of spinal disc and vertebral joint after a part or all of the nucleus pulposus tissue was removed from the disc of a living vertebrate, e.g. a human [2]. The spinal nucleus implant according to this prosthesis is a swellable plastic device capable of anisotropic swelling into a form of hydrogel implant with anisotropic deformability [5].

Hydrogels have been used in many fields due to their ease of preparation, their capacity of absorbing and releasing water, and the excellent oxygen permeability. Hydrogels are hydrophilic polymer molecules which are cross-linked by water. They do not dissolve, but swell in water. The capacity of hydrogels to absorb water is enormous and can be as much as 1000 times the weight of the polymer [2, 3]. The amount of water adsorbed by a hydrogel is expressed as the equilibrium water content (EWC) and is defined as:

EWC = (Weight of water in the gel/
/Weight of the hydrated gel) x 100%

Hydrogels have been widely used in the manufacture of many soft implants. Many commercial soft contacts are based on poly (2-hydroxyethylmethacrylate)(PHEMA) more commonly referred to as poly(HEMA), which has an EWC of 40%.

Poly (HEMA) is still the most commonly used material for medical applications such as contacts lenses [5]. It has the advantage of high oxygen premeability together with flexibility which is related to its adequate water content.

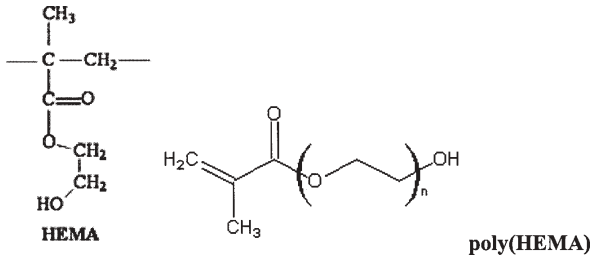

Fig.2 The HEMA hydrogels

The two monomers, for polymer HEMA formation, reaction following the schema:

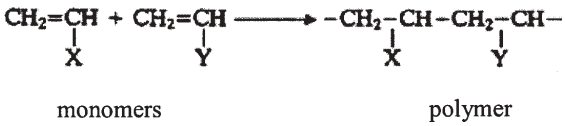

Fig.3 The conversion of monomers in polymer

First material used for this study is the pHEMA and the other material, which is used is a copolymer of HEMA and MMA. This material (referred to as Copolymer here after) has an extra hydroxyl group attached to it, which can absorb water because of its hydrophilic nature.

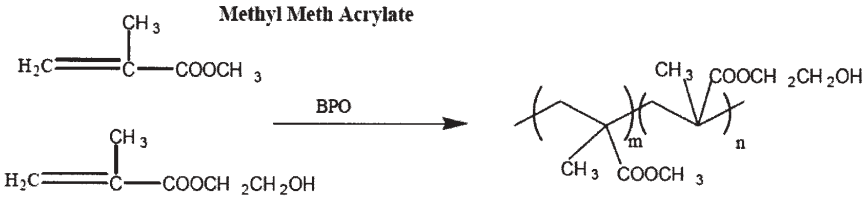

Fig.4 The reaction for HEMA polymer formation

Methods for testing

The purpose of this study, as explained earlier, was to show that HEMA/MMA copolymer is suitable for implantable intervertebral disc prosthesis. This copolymer is a polymer of HEMA and MMA monomers. In this research HEMA percentage in the copolymer was varied from 0% to 60%.

To show that these two polymers are suitable for intervertebral disc prosthesis two types of tests were done:

-the tensile tests;

-the saturation tests

Bulk material tests were basically tensile tests. Tensile tests on bulk material were done on specimens made out of copolymer with varying percentages of HEMA. The tests were done on samples with HEMA percentage of 0, 5, 10, 15, 20, 30, 40, 50, 60%. Each percentage samples were tested for both dry and soaked state.

For the bulk material test, standard test method for tensile properties of plastics was used. The samples were tested on a Universal Testing Machine, which has a load cell of maximum capacity 5000N, and a linear variable differential transformer type of extensometer. This extensometer has a minimum span of two inches with a maximum strain-measuring limit of two inches.

The wet samples were soaked for 54 days in a saline solution. The weight of these samples was measured (at the end of 40 days) at an interval of 2 days. When their weight stopped increasing, it was assumed the samples were fully hydrated (saturated) with water.

This copolymer of MMA and HEMA is expected to absorb water on exposure to 0.85% saline solution and become soft (decrease in modulus of elasticity). This softening will absorb the micro-motions and hence absorb the resulting loosening. This tendency to absorb water is expected to increase with increase in percentage of HEMA.

Objectives

To show that the copolymer absorbs water and becomes softer on water absorption.

To characterize the material properties of copolymer (Bulk Material samples) for:

a. Modulus of elasticity

b. Tensile strength.

Formulae used for calculations

The formulae that were used for various calculations are explained below: -

1. Modulus of Elasticity:

$$E = \frac{P}{\Delta L} \times \frac{L}{A}$$

where: load (P) ; elongation (ΔL); length (L); area of cross section (A).

Breaking Strength:

The ratio of maximum load that the sample can bear and the original area of the cross-section give the breaking strength.

$$\sigma_{br} = \frac{P_{br}}{A}$$

where: breaking load (P_{br}) ;area of cross section (A).

Results and discussion

Tensile tests have been performed for two types of samples—bulk material samples and structure sample. All these tests were conducted for different percentages of HEMA. The percentage of HEMA was varied from 0% HEMA to 60% HEMA. Each percentage samples were tested for both dry and soaked state.

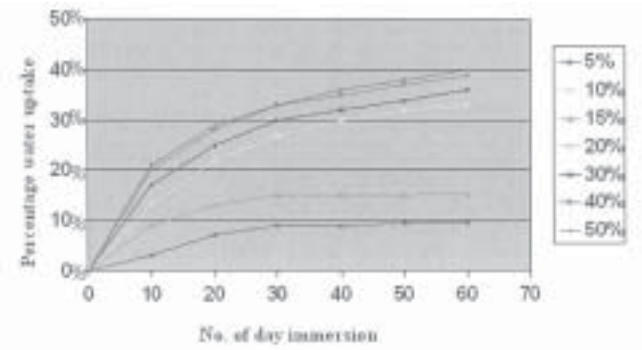

Fig..5 The water sorption of HEMA/MMA

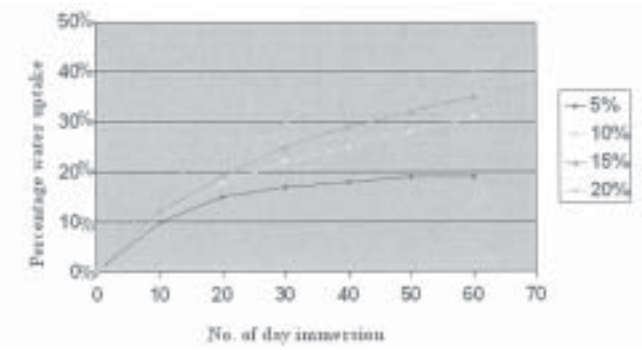

Fig..6 The water sorption of pHEMA

Summary of Bulk Material Sample Results

These points below summarize the result of sample tests. HEMA percentage increases from 0 % to 60 %.

Modulus of elasticity decrease from 1.9 GPa to 1 GPa for wet samples.

Breaking strength decrease from 35 MPa to 19 MPa for wet samples.

Note that breaking strength of 5% and 50% HEMA had an odd behavior of higher strength than expected.

Summary of Structure Sample results

Breaking strength decreases till 15% and then increased for 20% dry HEMA samples.

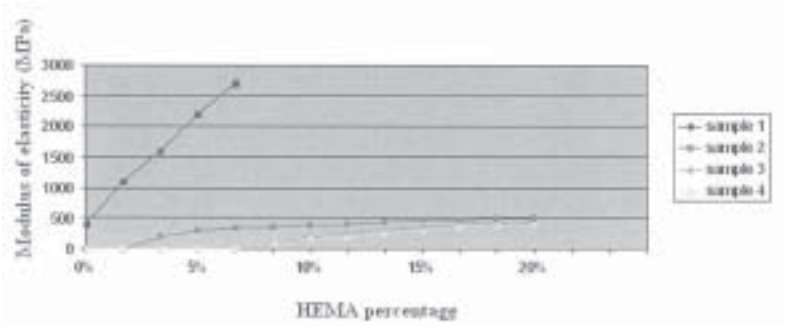

Fig..7 Modulus of elasticity pHEMA

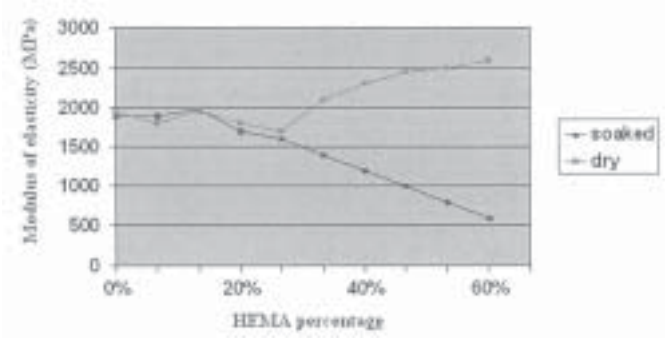

Fig..8 Modulus of elasticity HEMA/MMA

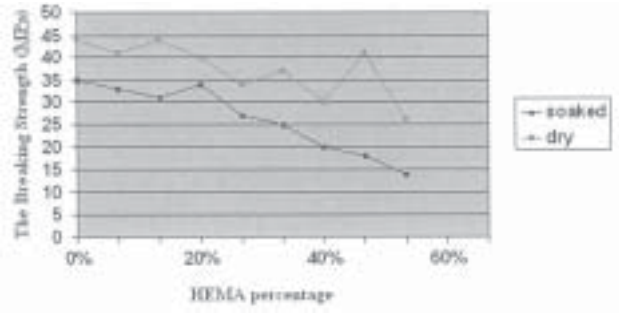

Fig..9 Breaking strength HEMA/MMA

Breaking load for wet samples (between 100 and 450) was in general less than that of dry samples (between 600 and 800

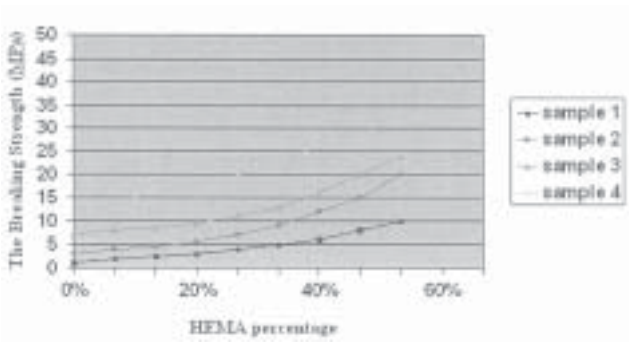

Fig.10 Breaking strength pHEMA

Summary of observations

- modulus of elasticity for soaked bulk material decreases;
- breaking strength for soaked bulk material decreases;
- modulus for dry bulk material samples increases.
-breaking strength of dry bulk material samples decreases;
- breaking strength of soaked structure sample decreases.;
- breaking strength of dry structure sample increases.

Conclusions

Both the modulus and tensile strength decrease with increase in the HEMA percentage for soaked bulk material samples. Whereas for dry bulk material samples modulus increases and breaking strength percentage elongation decreases with increase in HEMA percentage.

For soaked structure samples breaking strength decreases however with increase in HEMA percentage.

Increase in breaking strength was not observed in 50% and 60% HEMA structure samples.

All this put together leads to the conclusion that increasing HEMA percentage definitely makes soaked copolymer soft.

This decrease in modulus of elasticity indicates that this copolymer is better suited to absorb micro-motions if used in intervertebral disc replacements. Reduced micro-motions will eliminate loosening and, as a result, makes it a better material for the implant. The only associated disadvantage is the reduced breaking load. An optimum was found for breaking load at 40% HEMA.

It can be concluded that 40% HEMA/MMA copolymer is the best option. This material will take more loads and will absorb more energy. This is speculated that 40% HEMA will increase the life of intervertebral disc prosthesis by reducing loosening and brittle failure in intervertebral disc replacement.

References

1.BERTAGNOLI R, SACHS BL, RAY CD, PIMENTA L., Modified surgical technique for implantation of prosthetic disc nucleus devices. Presented at the International Meeting of Advanced Spine Techniques, Paradise Island, Bahamas, July 2001

2.GHI, PHUONG Y., HILL, DAVID J. T., WHITTAKER, ANDREW K., 1H NMR Study of the States of Water in Equilibrium Poly(HEMA-co-THFMA) Hydrogels. Biomacromolecules, 3, nr. 5, 2002, p. 991

3.MALAK, MARK, HILL, DAVID J. T., WHITTAKER, ANDREW K., Water sorption into poly[(2-hydroxyethyl methacrylate)-co-(1-vinyl-2-pyrrolidone)]at 310 K. Polymer International (2003), 52(11), 1740-1748.

4.HILL, DAVID J. T., Chowdhury, Mohammad; Ghi, Phuong Y.; Moss, Naomi G.; Whittaker, Andrew K., Water diffusion in methacrylate based copolymer hydrogels of 2-hydroxyethyl methacrylate. Macromolecular Symposia (2004), 207(Fundamentals and Applications of Polymer Gels), p. 111

5.CORKHILL P . H ., HAMILTON C. J ., TIGHE B . J., The Design of Hydrogels for Medical Applications', Critical Reviews in Biocompatibility, **5,** 1990, p. 363

6.CRETAN M., GRIGORAS S., HANGANU L., STAMATE V., IANUS G., Mat. Plast., 3, 2007, p.217

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