Biodegradable pHEMA containing graphene oxide for blood contacting applications

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Abstract

Blood contacting devices are widely used for the treatment of cardiovascular diseases. Small diameter vascular grafts (SDVG) (Ø<5mm) are often required, for instance in coronary or peripheral artery disease, as a strategy to reestablish the blood flow. However, the lack of a biomaterial to successfully replace the native small diameter vessels, avoiding infection and thrombus formation, demands improvements in this field [1, 2]. Our group has recently demonstrated that poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogels may be produced with high-strength and stiffness by combining it with graphene oxide (GO) [3], enabling its use as an inert SDVG.
The present work aims to develop a post-implantation tissue engineering approach for SDVG applications. For that, a new degradable biomaterial was designed by developing a degradable pHEMA (d-pHEMA) in combination with GO to achieve improved mechanical properties.
d-pHEMA films were produced by adding a degradable cross-linker pentaerythritol tetrakis(3-mercaptopropionate) (0.25-0.75wt.%), named as tetrakis, to a previously described formulation with and without a non-degradable cross-linker (tetraethylene glycol dimethacrylate, TEGDMA) [4]. Polymerization of all formulations was confirmed by FTIR, where no evidence of unreacted HEMA monomers (C=C; 1635 cm^{-1}) were observed. Similarly, water uptake and optical contact angle have demonstrated that tetrakis presence does not induce significant changes on swelling and hydrophilicity (~40°) of the native pHEMA, maintaining pHEMA hydrogel-like and non-fouling behaviors. This was also confirmed *in vitro* in a cell adhesion assay, where no human umbilical vein endothelial cells (HUVECs) adhered to d-pHEMA nor d-pHEMA/GO materials surface, after 1 and 7 days.
In vitro degradation studies showed that d-pHEMA with 0.75% Tetrakis (0.75T) totally disappear after 6 months, contrarily to other formulations. This was also verified *in vivo* in chorioallantoic membrane (CAM) assays, where 0.75T samples disappeared. Upon GO incorporation, the stability of the samples increased. The 24h degradation products were assessed using HUVECs, where no cytotoxicity was observed. These results are promising regarding a future application in SDVG, once d-pHEMA is cytocompatible with HUEVCs.
Mechanically, it was shown that incorporation of tetrakis decreased the young modulus and tensile strength (UTS). However, upon 1%GO addition, UTS increased to 0.06 MPa while keeping a strain of 39% (0.25T samples).
The new developed composite hydrogel d-pHEMA/GO has demonstrated to be biodegradable while keeping the essential properties for SDVG production.

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