STUDY OF A MAGNESIUM-BASED DEVICE FOR OCULAR APPLICATION

M. Ferroni (1), F. De Gaetano (1), N. Bono (1), M. Zonfrillo (3), G. Sferrazza (3), G. Candiani (1), M.G. Cereda (2), F. Boschetti (1)

1. Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Italy; 2. Department of Biomedical and clinical science, Sacco Hospital, University of Milan, Italy; 3. Institute of Translational Pharmacology, National Council of Research, Rome, Italy

Introduction

Wet age-related macular degeneration is the main cause of vision loss in developed countries. Millions of people are treated by intravitreal injections of anti-VEGF drugs [1]. We designed a device based on magnesium able to release doses of drug and avoid the burdens of repeated injections, due to its advantageous properties. In this work we present methods and results to characterize i) corrosion rate of Mg samples subjected to ocular shear stress levels, ii) in vitro biocompatibility and iii) drug stability in presence of Mg corrosion products.

Methods

In vitro corrosion of Mg samples: Corrosion tests on pure Mg samples were done at different time steps using a custom experimental setup up to 48 hours. The experimental flux was set to recreate on the upper surface of the specimens the same shear stress field evaluated by the numerical simulations of flow inside the vitreous chamber [2],[3]. Morphology and profile of all the specimens were evaluated and compared by SEM for the evaluation of the corrosion mechanisms.
In vitro biocompatibility test: The solution used for the treatment was prepared by dissolving the sterilized magnesium in 88.3 mL of serum-free DMEM solution in order to obtain a stock solution at a concentration of 0.2 µg/ml. Murine fibroblasts (3T3-NIH) and immortalized human keratinocytes (HACAT) cell lines were used to evaluate the biocompatibility.
Cells were grown in DMEM medium supplemented with 10% FBS in a 37 °C humidified atmosphere of 5% CO2. For Trypan blue test, 150'000 cells/well were seeded in 6 wells plate. For MTT test, 25'000 cells/well were seeded in 96 wells plate. After 24h, the culture medium was removed and replaced with medium conditioned at different concentrations.
Magnesium and anti-VEGF interaction: A customized indirect ELISA protocol was developed for evaluating the interaction between anti-VEGF drug (bevacizumab) and pure magnesium. Mg samples were prepared, dry sterilized and dissolved in a volume of BSS equal to 40 mL. Half of the solution was used for the determination of Mg content by ICP-OES analytical technique. The second half of solution was used for the interaction tests and analyzed at different time periods (0-1-7-14 days).

Results

In vitro corrosion of Mg samples: SEM images of Mg samples demonstrated uniform corrosion confirmed by CLSM data acquired during the experimental corrosion. The presence of localizations was mainly due to defects related to the manufacturing process. The corrosion rates evaluated in three fluid-induced shear stress (FISS) conditions were 1.9, 2.7 and 3.4 µm/day (Figure 1).
In vitro biocompatibility: The results obtained showed that Mg extracts did not induce cell death in both cell lines. No significant toxic effects were observed at the various concentrations 24h/48h after treatment compared to untreated control.
Magnesium and anti-VEGF interaction: Changes in averaged values of bevacizumab activity in contact with magnesium are always less than or equal to 10% if compared to the control case, represented by the drug activity itself, not in contact with magnesium, at the same time points (0, 1, 7, 14 days).

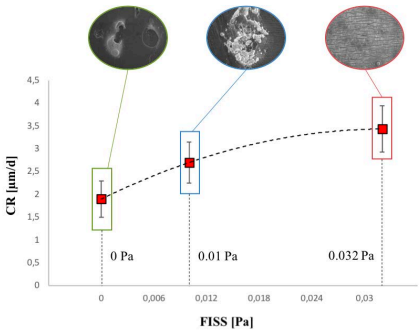

Figure 1: Trend of corrosion rate of Mg biodegradation.

Discussion

We demonstrated the feasibility of magnesium as drug carrier for the treatment of maculopathy or potentially other eye pathologies, developing a quantitative method to test whether the drug stability is affected by the presence of Mg corrosion products. Mg samples showed uniform corrosion and absence of toxic aspects. Finally, magnesium does not alter the bevacizumab stability. The Our results provide the scientific basis for continuing with the subsequent characterization in view of the clinical use of the device.

References

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