STUDY OF A MAGNESIUM-BASED DEVICE FOR OCULAR APPLICATION

M. Ferroni (1), F. De Gaetano (1), N. Bono (1), A. Stocchino (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. Department of Civil, Chemical and Environmental Engineering, University of Genoa, 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) corrosion of prototypes 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 until 48 hours. The experimental flux was set to recreate on the upper surface of specimens the same shear stress field evaluated by the numerical simulations of flow inside the vitreous chamber [2]. Morphology and profile of all the specimens were evaluated and compared by SEM for the evaluation of the corrosion mechanisms.
In vitro test on prototype: Scaled prototypes of the device were provided in JDBM alloy [3]. The specimens were subjected to a SEM analysis before and after the tests. Prototypes were inserted inside an experimental setup, reproducing the ocular kinematics, in order to simulate the device corrosion in the eye by means of a brushless electric motor, able to impose sinusoidal movements. The influence of six different solutions reproducing the vitreous humor, pH and the condition of open/closed system on the corrosive process were investigated. After the tests, corrosion products were removed to evaluate the Mg bulk-only corrosion.
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 solution was used for the determination of the Mg content, performed with the analytical technique of ICP-OES. 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.
In vitro test on prototype: Results on corrosion are given by SEM images which show the grain structure after six-days of dynamic stimuli (Figure 1). Closed environment induces a slower corrosion as a consequence of the weak formation of hydrogen bubbles and the absence of gas exchange that takes place through the RCS complex. The pH curves increase and reach the plateau value after two hours of test. BSS is the most suitable solution since its similar concentration of chlorine ions with respect to the vitreous one.
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).

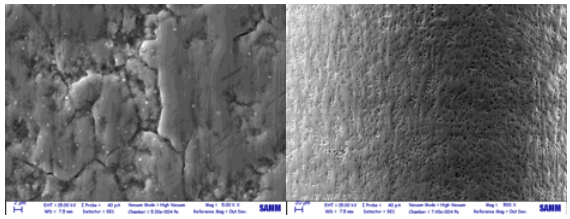

Figure 1: SEM images of the surface of the prototype after the test and the removal of corrosion products.

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 may be affected by the presence of Mg corrosion products. Mg samples and JDBM prototypes showed uniform corrosion. Several conditions (e.g. pH changes) were studied and will be considered for the quantitative analyses of prototype corrosion.

References

1. Choonara et al, J Pharm Sci, 99:2219–2239, 2010.
2. Ferroni et al, Ann Biomed Eng, 46:2091-2101, 2018.
3. Mao et al, Nanoscale, 5:9517-9522, 2013.

Acknowledgements

This study was funded by the Italian Ophthalmological Society (SOI). Mg samples and prototypes were generously given by Prof. Guangyin Yuan, School of Material Science and Engineering, Shanghai Jiao Tong University, China.