Drug Release from Multicomponent Implant

L. Nikkola[1], P.Viitanen[1] and N. Ashammakhi[1]
[1] *Institute of Biomaterials, Tampere University of Technology, Tampere, Finland*

INTRODUCTION: In our previous study (Viitanen et al. 2005) we have reported on developing DS releasing bioabsorbable rods. However, their drug release properties were unsatisfactory. We have thus assessed the use of sintering technique of enhancement of drug release in the current study.

METHDOS: Melt extruded PLGA 80/20 rods were compounded 8wt-%DS. Three different components were produced by self reinforcing (SR) some of compounded 8wt-%DS rods and sterilize some of the SR-rods. These three different rods were sintered with heat and pressure to form one multicomponent rod. Thermal properties were analyzed using differential scanning calorimetry (DSC) to determine glass transition temperature (Tg), melting temperature (Tm) and heat of fusion (ΔH). Drug release measurements were performed using UV-Vis spectrophotometer. There were three different specimen groups: A1 constructed from even parts of components, B1 and B2 from 47 volume-% of compounded and 32 volume-% of SR and 21%-volume of sterilised SR rods. B2 specimens were sterilized. Five parallel samples of three different specimen groups (A1, B1, and B2) were measured first at 6 hour intervals then on daily basis and later about three times a week. Mechanical strength was measured during two weeks after which the components disintegrated each other.

RESULTS: Release rate consisted of three different phases: 1) sharp start peak, 2) second smoother peak, and 3) the last smooth peak (Fig. 1). The form of the profile depended on the fractions of different components.

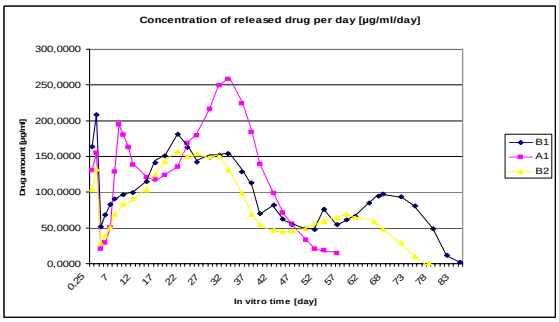

Fig. 1 Drug release profiles of the three specimen groups.

Released DS concentrations reached local therapeutic levels and maintained at that stage for 24-36 days depending on the fraction of different components. A11 DS was released from the rods during 50-70 days. Notable was also the accelerative effect of sterilization to the release.

The drug release profiles of initial components and sintered multicomponent differs from each other dramatically. It is easily seen that the drug release of multicomponent implant is more stable and begins earlier, which are the properties desired.

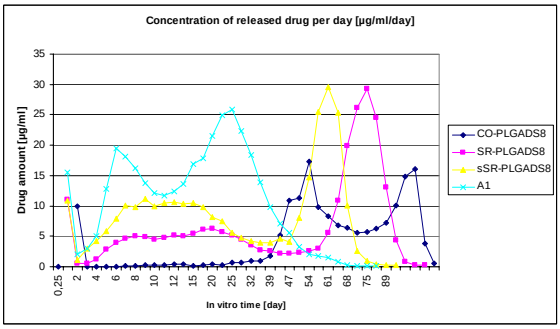

Fig 2. Comparison of drug release profiles of initial components to sintered multicomponent implant.

Initial shear strength was 82MPa and it decreased to 15MPa during two week in hydrolysis when after the components disintegrated. The mechanical attachment accomplished by sintering was sufficient although the components disintegrated too fast.

CONCLUSIONS: By sintering different PLGA/DS components, which have different release rates it is possible to construct a truly controlled release implant for bone fixation with anti-inflammatory properties.

REFERENCES: P. Viitanen, E. Suokas, P. Törmälä, N. Ashammakhi. Release of diclofenac sodium from polylactide-go-glycolide 80/20 rods. Journal of Materials Science: Materials in Medicine as permanent record of the 10th International Meeting on Polymers in Medicine & Surgery (submitted).

ACKNOWLEDGEMENTS: Research funds from the European Commission (EXPERTISSUES project NMP3-CT-2004-500283), Technology Development Center in Finland (TEKES) and the Academy of Finland (Center of Excellence 73948) are greatly appreciated.