**Controlled Drug Release from Bioerodible Hydrogels Based on Poly(ethylene glycol) and Sebacic Acid**

Jinku Kim, Lichun Lu, Bradford L. Currier, & Michael J. Yaszemski
Tissue Engineering and Polymeric Biomaterials Laboratory, Departments of Orthopedic Surgery and Biomedical Engineering, Mayo Clinic College of Medicine, Rochester, MN 55905

## Introduction

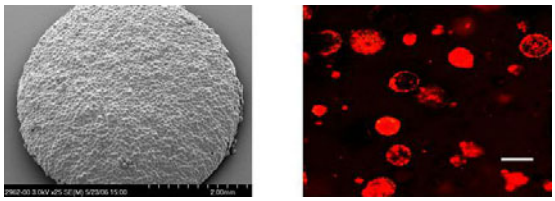
Synthetic hydrogels have become increasingly attractive candidates as drug carriers mainly due to reproducibility and better control of their final properties such as drug release rate and biodegradability than natural hydrogels [1]. However, synthetic hydrogels have certain limitations as drug delivery vehicles including handling problems or structural instability due to low mechanical properties [2]. Recently, we have developed poly(ethylene glycol) (PEG) based hydrogel, PEG sebacate diacrylate (PEGSDA) which is less swellable and has enhanced mechanical strength, compared with conventional PEG based hydrogel such as PEG diacrylate (PEGDA) [3]. In this study, we examined how different drug (we're using a model drug here not a protein) incorporation methods can affect the release profiles of the molecule encapsulated in the PEGSDA hydrogels.

## Materials and Methods

PEGSDA was synthesized as described previously [3]. PLGA microspheres were fabricated using a double emulsion techniques [4] and characterized by scanning electron microscopy and confocal laser scanning microscopy. Texas red dextran (TRD), a model drug, was encapsulated directly into either PEGSDA solution or PEGSDA solution containing $Mg(OH)_2$ (0.3% w/v) at 300 μg/g scaffold. The same amount of TRD was also encapsulated in 100 mg of PLGA microspheres which were then incorporated into PEGSDA solution. Disk shaped hydrogel scaffolds were incubated in PBS at 37 °C for up to 35 days. TRD release profiles were measured by UV absorption at 595 nm in a spectrophotometer.

## Results and Discussion

SEM images of PLGA microparticles containing TRD showed spherical particles ranged from 1 to 130μm with an average diameter of 85 ± 30 μm. Light and confocal microscopy revealed that microspheres containing well-distributed TRD inside the microsphere were evenly dispersed throughout the hydrogel (Fig. 1).



A B

Figure 1. (A) SEM image of a hydrogel disc containing PLGA microspheres and (B) Confocal micrograph of TRD distribution in the hydrogel phase (scale bar = 100 μm).

Release kinetics of TRD from different PEGSDA hydrogel carriers were determined by incubating them in PBS at 37°C over the 35-day time period (Fig. 2). PEGSDA alone and PEGSDA incorporated with PLGA microspheres exhibited initial burst release and subsequent sustained release profiles. PLGA microsphere containing hydrogel showed much greater TRD release compared with hydrogel alone carrier likely due to the difference of diffusion rate and hydrophobic interaction between the incorporated molecule and carriers. $Mg(OH)_2$ incorporated hydrogel showed greater sustained release profile compared with PEGSDA alone. $Mg(OH)_2$ is known to prevent protein aggregation and acid-catalyzed hydrolysis both of which are detrimental to protein stability[5]. These results indicate that drug release profiles can be controlled by the encapsulation methods. These carriers will be further assessed to see how these methods could affect bioactivities of various growth factors used in tissue engineering such as bone morphormetric proteins (BMPs).

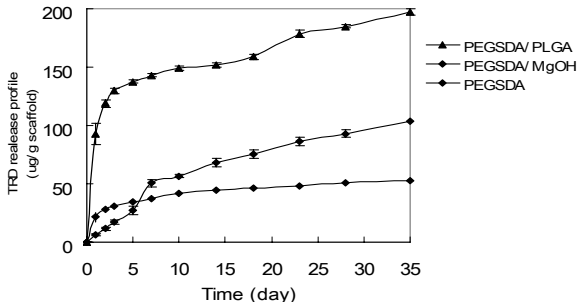



Figure 2. TRD release profiles from different PEGSDA carriers

## Conclusions

We examined the feasibility of various PEGSDA hydrogels as drug delivery carriers. Different drug encapsulation methods were examined. PLGA microsphere containing hydrogel exhibited greater initial burst release whereas $Mg(OH)_2$ incorporated hydrogel showed minimal initial burst release and subsequent greater sustained release up to 35 days, as compared with PEGSDA hydrogel alone. These results show that PEGSDA based carriers could be used as local drug carriers for various biomedical application such as tissue engineering.

## References

[1] Drury JL and Mooney DJ, Biomaterials, 24, 4337, 2003
[2] Hoffman AS, Adv Drug Deliv Rev, 43, 3, 2002
[3] Kim J et al., submitted , 2006
[4] Kempen DHR et al., J Biomed Mater Res, 77A, 103, 2006
[5] Zhu et al., Nat Biotechnol, 18, 52, 2000

## Acknowledgments

Work supported by Mayo Foundation and NIH grants R01 AR45871 and R01 EB003060.