

**Supplementary information**

**Incorporation of simvastatin in PLLA membranes for guided bone regeneration: effect  
of thermal treatment on simvastatin release**

*Antonio G. B. Castro, Dennis W. P. M. Löwik, Mies J. van Steenbergen, John A. Jansen,  
Jeroen J. J. P. van den Beucken, Fang Yang\**

M.Sc. A. G. B. Castro, Prof. Dr. J. A. Jansen, Dr. J. J. J. P. van den Beucken

Department of Biomaterials, Radboudumc, Philips van Leydenlaan 25, Nijmegen, 6525 EX,  
The Netherlands

Mies J. van Steenbergen

Utrecht Institute for Pharmaceutical Sciences(UIPS), Utrecht University, 3584 CG Utrecht,  
The Netherlands

Dr. Dennis W. P. M. Löwik

Bio-organic Chemistry, Institute for Molecules and Materials, Radboud University Nijmegen,  
Heyendaalseweg 135, Nijmegen, 6525 AJ, The Netherlands

\*Dr. F. Yang

E-mail: [fang.yang@radboudumc.nl](mailto:fang.yang@radboudumc.nl)

Department of Biomaterials, Radboudumc, Philips van Leydenlaan 25,  
Nijmegen, 6525 EX, The Netherlands

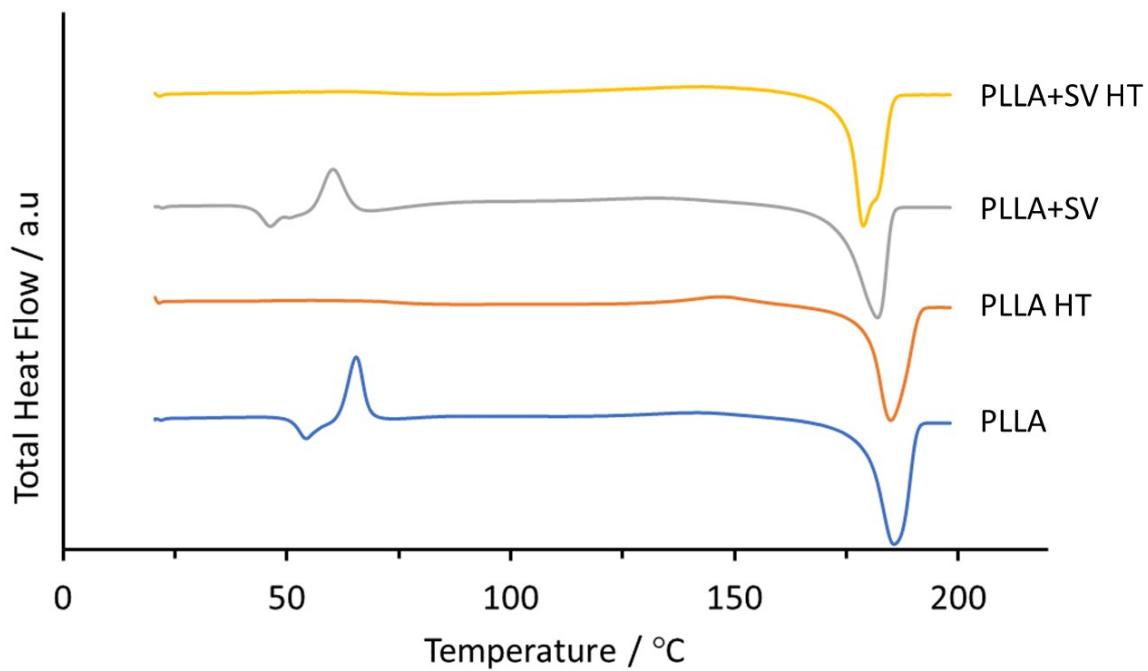


Figure S1. Modulated DSC spectra for the different electrospun membranes.

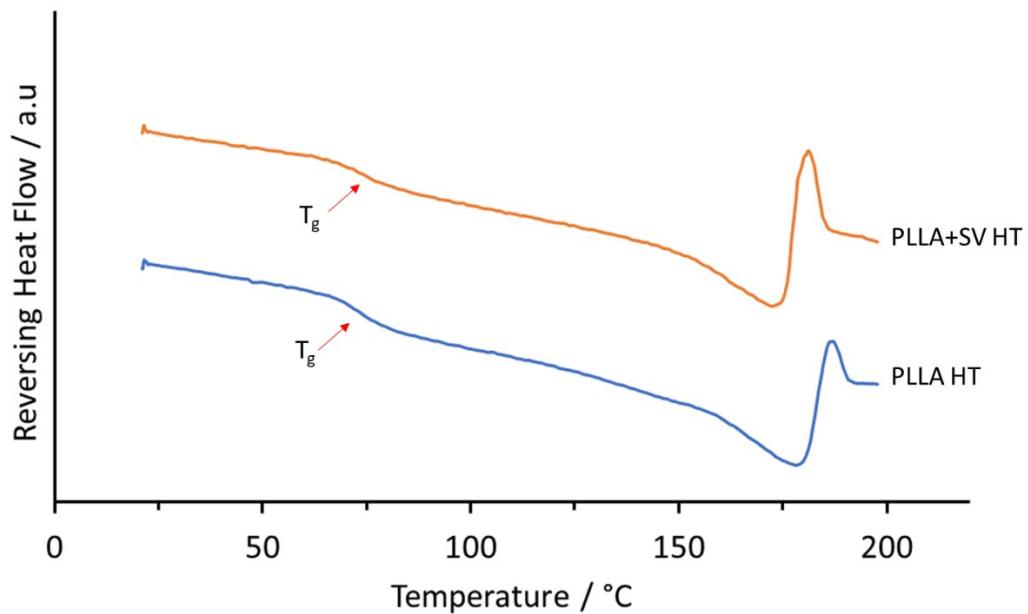


Figure S2. Modulated DSC spectra (reversing signal) for PLLA HT and PLLA+SV HT membranes.

As described in Table S1, SV incorporation led to a small decrease in the values of glass transition temperature ( $T_g$ ) and cold crystallization temperature ( $T_{cc}$ ), related to a plasticizing effect common when drugs are added to polymeric materials.<sup>[1, 2]</sup> Membranes subjected to the thermal treatment showed an increase in  $T_g$  values, which is related to a higher organization and rigidity of the polymeric chains, a consequence of the higher crystallinity present on these membranes.

Table S1. Thermal properties of the electrospun membranes.

Group	Crystallinity / %	$T_g$ / °C	$T_{cc}$ / °C	$T_m$ / °C
PLLA	42.0±7.76	53.6±1.07	66.2±0.62	185.8±0.15
PLLA HT	58.3±4.40	73.1±0.32	-----	184.8±0.21
PLLA+SV	38.4±3.04	46.3±0.12	60.6±0.15	182.1±0.06
PLLA+SV HT	61.5±1.06	73.3±1.04	-----	178.8±0.10

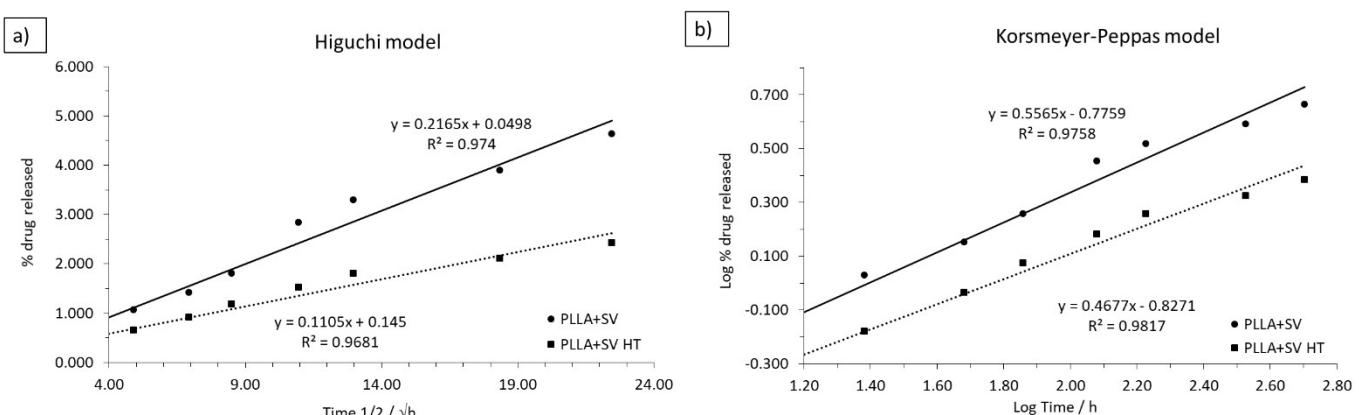
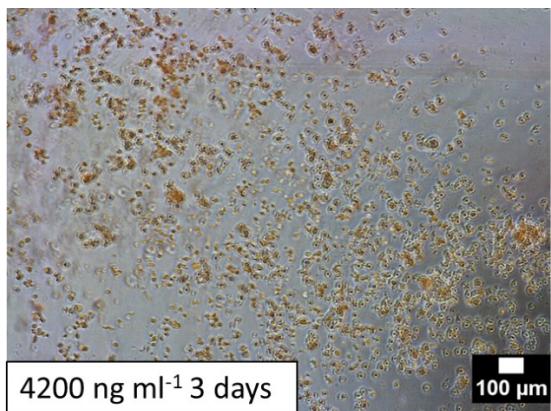
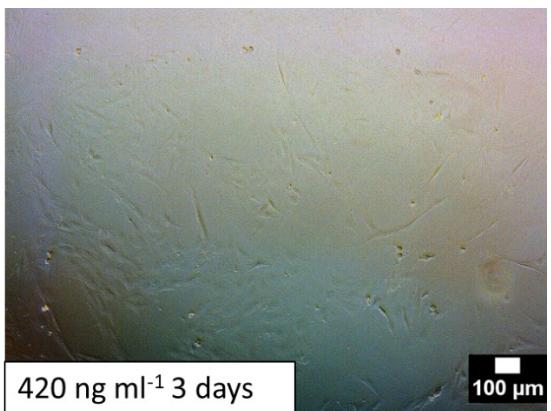


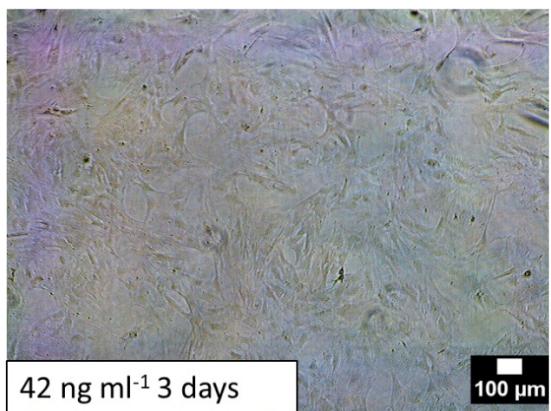
Figure S3. Fitting of the drug percentage released for both membranes according to a) Higuchi model b) Korsmeyer-Peppas model.



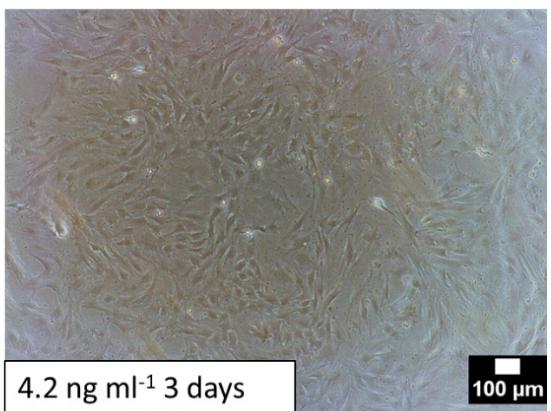
4200 ng ml<sup>-1</sup> 3 days



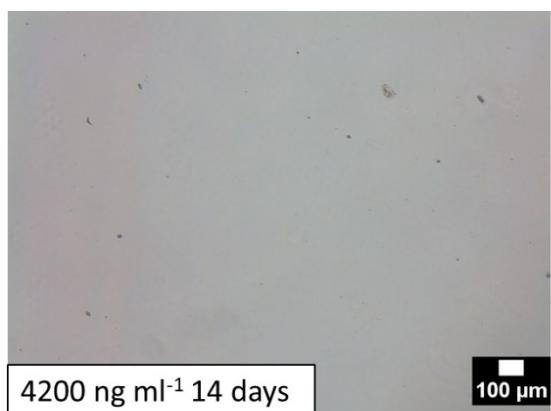
420 ng ml<sup>-1</sup> 3 days



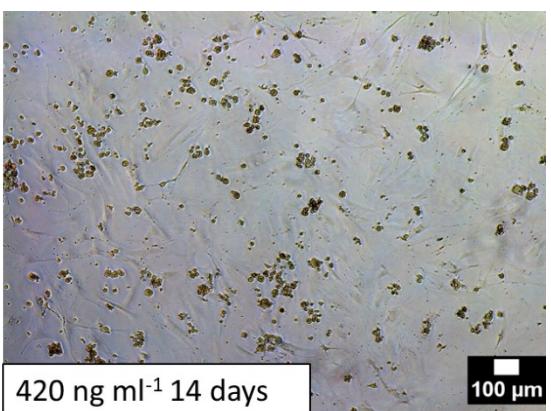
42 ng ml<sup>-1</sup> 3 days



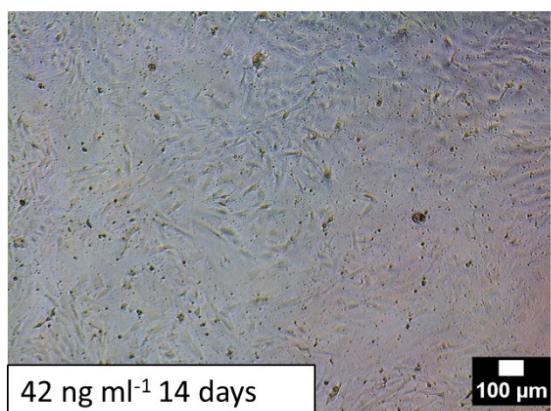
4.2 ng ml<sup>-1</sup> 3 days



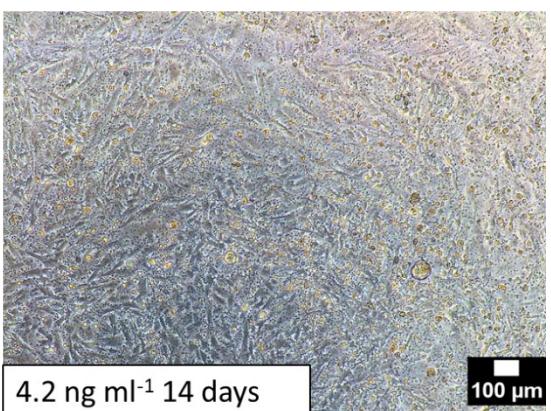
4200 ng ml<sup>-1</sup> 14 days



420 ng ml<sup>-1</sup> 14 days



42 ng ml<sup>-1</sup> 14 days



4.2 ng ml<sup>-1</sup> 14 days

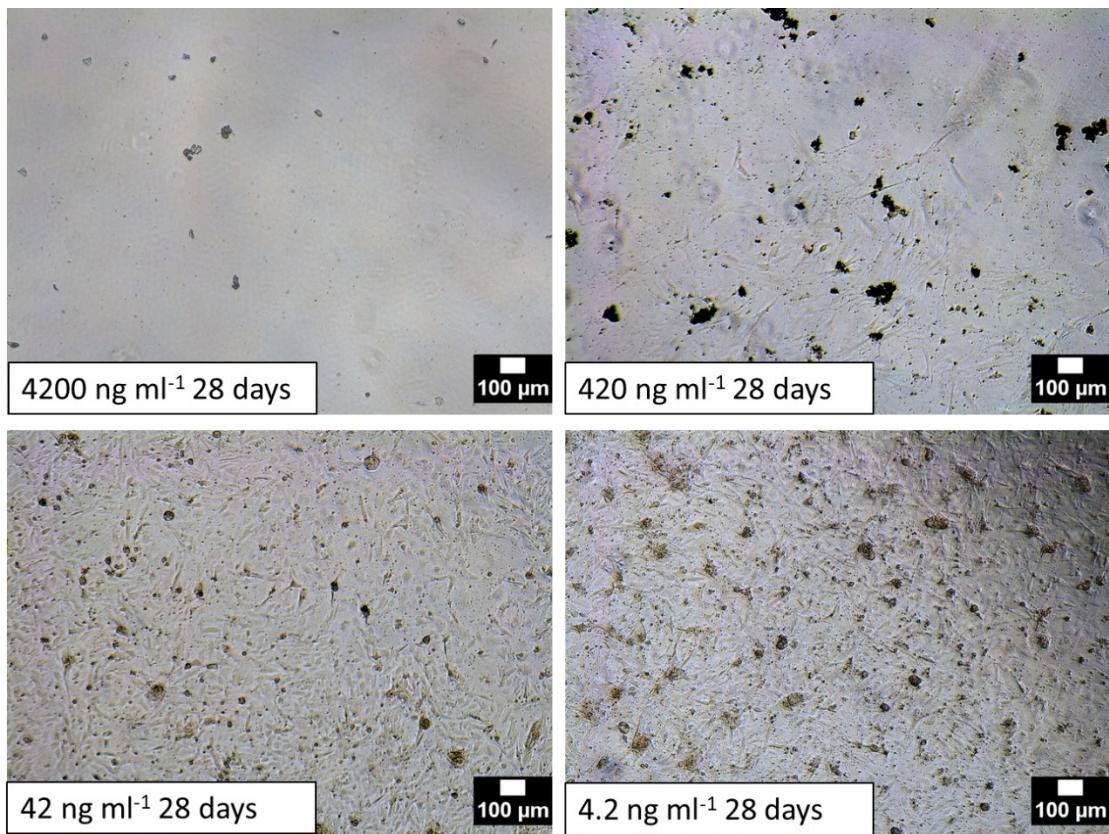


Figure S4. Optical microscope images of rat bone marrow stromal cells (rBMSCs) cultured with a proliferation medium containing different concentrations of simvastatin, after 3, 14 and 28 days of culture.

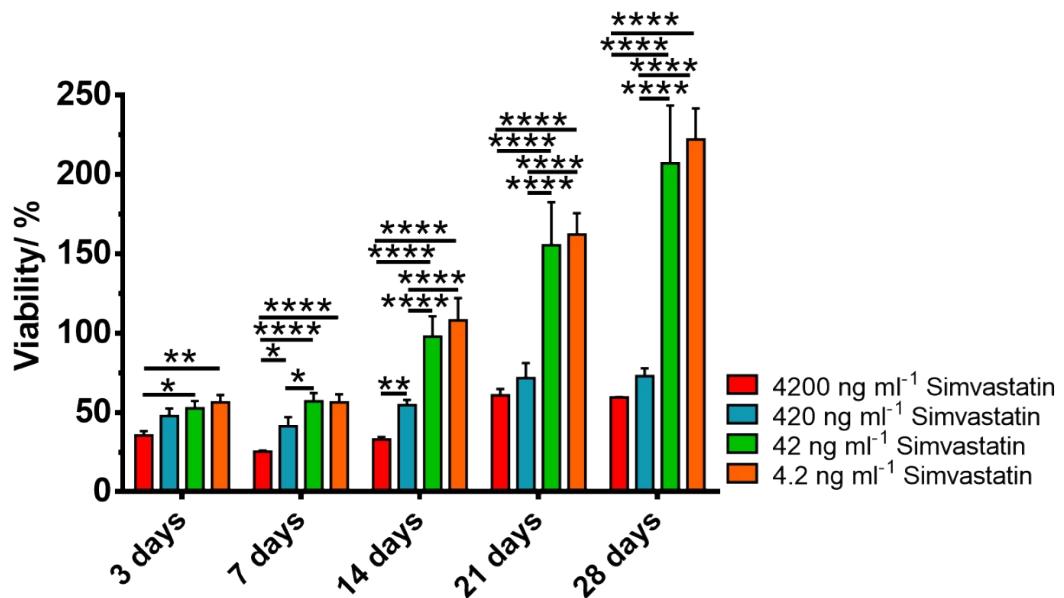


Figure S5. AlamarBlue test for rBMSCs culture with proliferative medium containing different concentrations of simvastatin. \*p<0.05, \*\*p<0.01, \*\*\*\*p<0.0001. Viability percentages (%) are relative to the positive control (rBMSCs cultured in an osteogenic medium).

## References

1. S.T. Hsu and Y. L. Yao, *J. Appl. Polym. Sci.*, 2013, **130**(6), 4147-4156.
2. J. Yao, S. Zhang, W. Li, Z. Du and Y. Li, *RSC Adv.*, 2016, **6**(1), 515-521.