Supporting information:

Biodegradable and multilayered drug delivery coatings composed of daidzein-loaded PHBV microspheres embedded in polymer matrix by electrophoretic deposition

Qiang Chen ^{‡a,b}, Wei Li ^{‡b⊥}, Qingqing Yao ^c, Ruifang Liang ^d, Rosalina Pérez-Garcia ^e, Josemari Munoz ^e, Aldo R. Boccaccini ^{*b}

a. Key Laboratory for Space Bioscience and Biotechnology, School of Life Sciences, Northwestern Polytechnical University, Xi'an, Shaanxi 710072, China

b. Institute of Biomaterials, Department of Materials Science and Engineering, University of Erlangen-Nuremberg, Cauerstrasse 6, 91058 Erlangen, Germany

c. Institute of Advanced Materials for Nano-Bio Applications, School of Ophthalmology & Optometry, Wenzhou Medical University, Wenzhou, 270 Xueyuan Xi Road, Zhejiang 325027, China

d. Department of Internal Medicine 3 and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany

e. CIDETEC, Parque Tecnológico de Miramón, Paseo Miramón 196, 20009 San Sebastian, Spain

⊥ Current address: Institute of Biotechnology & Division of Pharmaceutical Chemistry and Technology, Faculty of Pharmacy, University of Helsinki, FI-00014, Helsinki, Finland

‡ These two authors share first co-authorship.

*Corresponding author: aldo.boccaccini@ww.uni-erlangen.de

Table S1: Parameters for optimizing the fabrication of PHBV microspheres, and the particle size of the prepared PHBV microspheres using each parameter combination. The particle sizes were given as mean \pm standard deviation.

Stirring rate	PHBV concentration	PVA concentration	Particle size	
(rpm)	(% w/v)	(% w/v)	(µm)	
3500	1	1	9.2 ± 2.2	
3500	3	2	12.9 ± 3.3	
3500	5	3	8.3 ± 3.6	
7000	1	2	2.5 ± 0.7	
7000	3	3	4.2 ± 0.9	
7000	5	1	4.7 ± 1.7	

11000	1	3	1.7 ± 0.3
11000	3	1	3.1 ± 0.7
11000	5	2	3.1 ± 0.6
7000	3	2	4.2 ± 1.0
7000	3	1	4.1 ± 1.5

Table S2: The protocol and composition of daidzein-containing culture medium applied to

 evaluate the cytoxicity of daizein to MC3T3-E1 and RAW 264.7 cell lines.

Sample code	1	2	3	4	5	6	7	8
C _{Daidzein} in DMSO (µg/ml)	5000	1000	200	40	8	1.6	0.32	0
$V_{\text{DMSO}}(\mu l)$	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
$V_{Culture medium}$ (µl)	99.5	99.5	99.5	99.5	99.5	99.5	99.5	99.5
<i>C_{Daidzein}</i> in final medium (µg/ml)	25	5	1	0.2	0.04	0.008	0.0016	0

* The final medium was prepared by mixing 0.5µl of daidzein-containing DMSO solution with 99.5µl standard culture medium.



Fig. S1: The influence of DMSO concentration in culture medium on the viability of MC3T3-E1 and Raw 26.7 cells by MTT assay, which shows that the critical DMSO concentration inducing toxic effect to the both cells is 1.25 vol%.



Fig. S2: Optical microscope images and particle sizes of PHBV microspheres prepared using different parameters. The particle sizes are given as mean \pm standard deviation.



Fig. S3. Surface and cross-sectional SEM images of different coating configurations in **Fig. 2**, (a, b) A-coating, (c, d) C-coating.



Fig. S4: Fitting of daidzein release from PHBV microspheres with different levels of drug loading using (a) Higuchi equation and (b) Peppas equation



Fig. S5: The effect of daidzein concentration on RAW 264.7 cell viability after 2 days of culture measured by MTT assay.