Adhesive Polyelectrolyte Complex Nanoparticles for the Delivery of Bone Therapeutic Drugs

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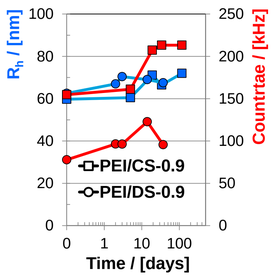
The therapy of fractures and defects in the systemically diseased hard tissue is one of the great challenges in medicine. Artificial allogenic bone substituting materials (BSM) are used for bone remodelling and tissue regeration, but have problems or fail in the case of systemic bone diseases osteoprosis (OP) and multiple myeloma (MM).
This work aims at the development of an adhesive nanoscaled carrier system for bone therapeutic drugs usable for the functionalization and improvement of BSM. We have chosen biocompatible polyelectrolyte complex (PEC) nanoparticles (NP) loaded by relevant therapeutics.

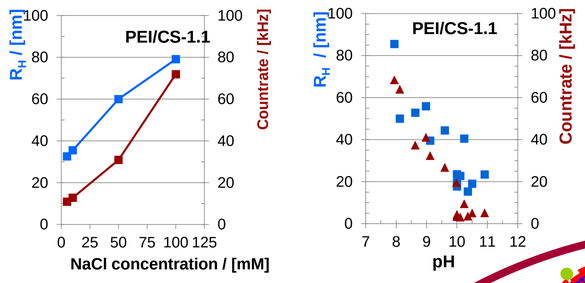
Colloid Stability

Time stability (aging)



Time dependence of countrate and particle radii of PEI/CS PEC NP.

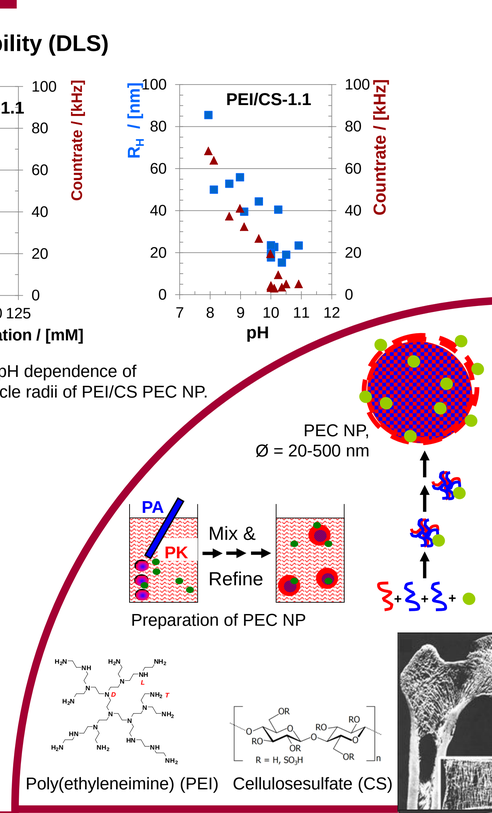
Salt and pH stability (DLS)

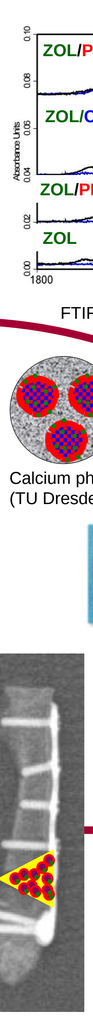


Ionic strength and pH dependence of countrate and particle radii of PEI/CS PEC NP.

Drug loaded PEC-NP
- Defined sizes 20 - 300 nm
- Defined net charge
- Colloid stability ≥ 1 month
- pH and salt influence

M. Müller, *Advances in Polymer Science* **2014**, 256, 197-260.

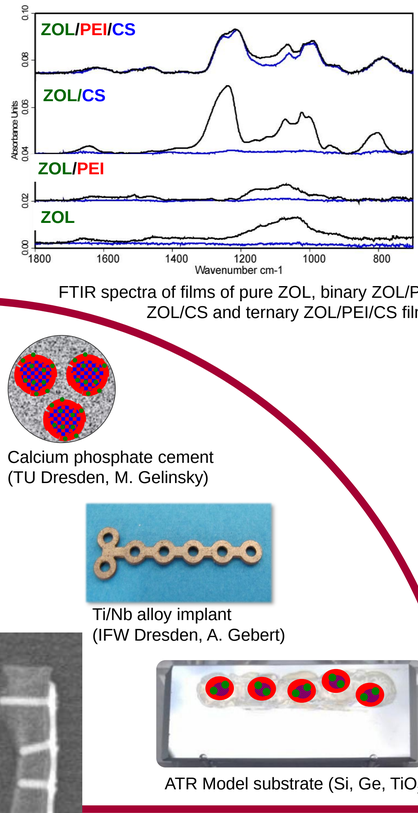




Calcium phosphate cement
(TU Dresden, M. Gelinsky)

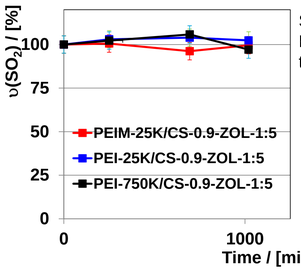
Ti/Nb alloy implant
(IFW Dresden, A. Gebert)

ATR Model substrate (Si, Ge, TiO_2)

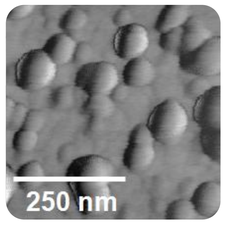


FTIR spectra of films of pure ZOL, binary ZOL/PEI, ZOL/CS and ternary ZOL/PEI/CS films.

Interfacial Stability



Stabilty of PEC/ZOL Films after contact to release medium.



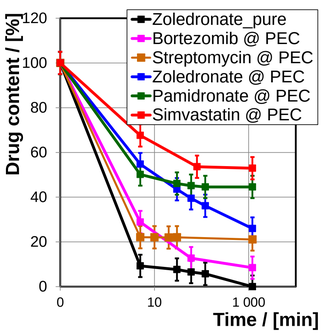
PEC NP @ Si

Drug loaded PEC-NP
- Adhesive stability of ternary drug/PEI/CS film (release medium).

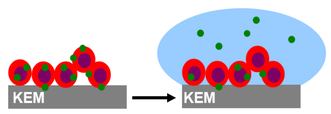
B. Torger, D. Vehlow, B. Urban, S. Salem, D. Appelhans, M. Müller, *Biointerphases* **2013**, 8:25.

Drug Release

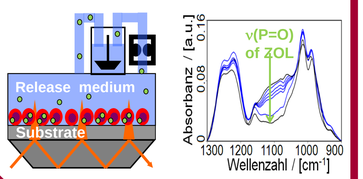
Variation of drugs



Release of various drugs from PEC NP.

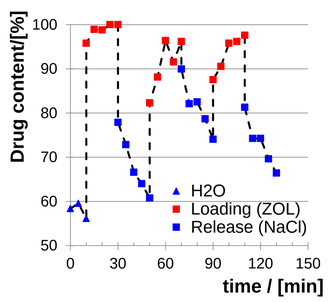


Drug Release from PEC NP films



in-situ-ATR-FTIR detection of drug release from PEC NP films

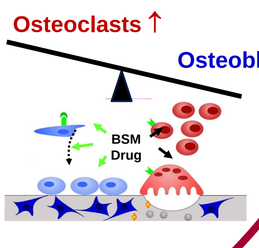
Periodic drug loading and releasing
@ PEC-NP films (ZOL @ PEI/CS)

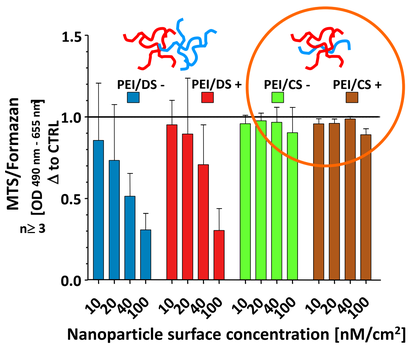


Drug loaded PEC-NP
- Release drugs in defined way
- Influence of drug & PEC system
- Recyclable drug delivery

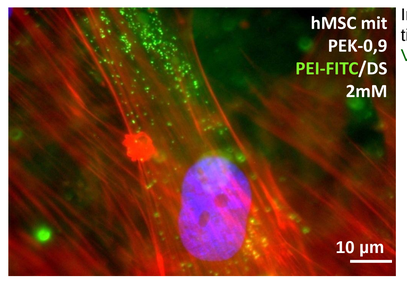
DE 10 2010 003 615.3
M. Müller, B. Keßler, *J. Pharm. Biomed. Anal*. **2012**, 66, 183.

Cell Compatibility





MTS (tetrazolium salt) assay (mitochondrial reductase) on human mesenchymal stromal cells (hMSC) cultured above PEC NP (TU Dresden, U. Hempel).



Immunofluorescence image on hMSC cultured above PECNP @ tissue culture PS dishes. (DAPI: nucleus, β-tubulin: focal adhesion, Vinculin: cytosceleton & PEC-FITC-NP)

Drug loaded PEC-NP
- Interact with hMSC and internalize
- Influence of PEC composition
- No influence of net charge

B. Woltmann, B. Torger, M. Müller, U.Hempel, *Int. J. Nanomedicine* **2014**, 9, 2205.

Co-operation within the IPF:
Program Area 1
Program Area 4

Co-operation
Technische Universität Dresden, Medizin. Fakultät, AK Prof. Gelinsky, AK Dr. Hempel
Universität Gießen, Universitätsklinikum, AK Prof. Schnettler
Universität Heidelberg, Universitätsklinikum, AK Prof. Goldschmidt
Deutsches Krebsforschungszentrum Heidelberg, AK PD Dr. Schwartz-Albiez
Leibniz-Institut für Festkörper- und Werkstoffforschung Dresden, AK Prof. Eckert

DRESDEN concept

IFW Leibniz-Institut für Festkörper- und Werkstoffforschung Dresden

SFB Transregio 79
Werkstoffe für die Geweberegeneration im systemisch erkrankten Knochen
Gießen, Heidelberg, Dresden

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