

DEVELOPMENT OF COHESIVE SELF-HEALING GELS BASED ON SELF-ASSEMBLY OF ORGANIC AND INORGANIC NANOPARTICLES

M. Diba^{1,2}, D. W. P. M. Löwik², J.C. M. van Hest², J. A. Jansen¹, S. C. G. Leeuwenburgh¹

¹ Department of Biomaterials, Radboud University Nijmegen Medical Center, Philips van Leydenlaan 25, 6525 EX Nijmegen, The Netherlands– e-mail: m.diba@dent.umcn.nl; j.jansen@dent.umcn.nl; s.leeuwenburgh@dent.umcn.nl

² Department of Bio-organic Chemistry, Radboud University Nijmegen, Heyendaalseweg 135, 6525 AJ Nijmegen, The Netherlands– e-mail: d.lowik@science.ru.nl; j.vanhest@science.ru.nl

Keywords: Colloidal gel, self-healing, nanoparticles, nanocomposite

ABSTRACT

Noncovalent bonds are often reversible and sensitive to external stimuli. Although noncovalent interactions are inherently weak and generally perceived as inadequate to construct macroscopic materials of sufficient integrity and cohesion, the emergence of nanotechnology has shown that the intrinsic weakness of noncovalent interactions can be compensated by maximizing the number of these bonds that work in concert. In that way, remarkably strong materials can be formed. Colloidal gels are an emerging and particularly attractive class of cohesive hydrogels. These materials allow for “bottom-up” design of functional materials by employing noncovalent interactions between micro- or nanoscale particles as building blocks to assemble into shape-specific bulk materials. In an attempt to explore the feasibility of using electrostatic and hydrophobic interactions between nanoparticles, it was recently observed that colloidal gels made of oppositely charged gelatin nanospheres were surprisingly cohesive, elastic and self-healing. In the current study, we aim to extend this concept towards self-healing colloidal gels by synthesizing organic nanoparticles that exhibit a strong affinity for inorganic nanoparticles using various types of bioinspired derivatization strategies. The organic nanoparticles impart flexibility and resilience to these gels, while the inorganic nanoparticles improve their hardness and rigidity.

1. INTRODUCTION

Generally, functional materials owe their integrity to irreversible covalent bonds. The irreversibility of these covalent bonds renders these materials incapable of self-healing since these bonds cannot be restored after rupture. In contrast, non-covalent bonds are often reversible and more sensitive to external stimuli. Although these noncovalent interactions are inherently weak and generally perceived as inadequate to construct macroscopic materials of sufficient integrity and cohesion, the emergence of nanotechnology has shown that the intrinsic weakness of non-covalent interactions can be compensated by maximizing the number of these bonds that work in concert. In that way, remarkably strong materials can be formed. Still, non-covalent synthetic methodology is only starting to emerge as a research field. In that respect, colloidal gels are an emerging and particularly attractive class of cohesive hydrogels.

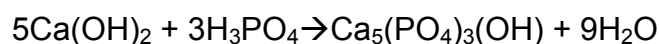
These materials allow for “bottom-up” design of functional materials by employing noncovalent interactions between micro- or nanoscale particles as building blocks to assemble into shape-specific bulk materials. Moreover, biomimetic strategies have shown to be promising approaches for development of advanced functional materials. Bone tissue is a nanostructured inorganic-organic composite and is one of the most striking examples of a self-healing material since it is able to continuously restore its integrity in response to damage. Studies have indicated that the nanostructure of bone as well as non-covalent interactions between its organic and inorganic phases are key factors determining its self-healing properties. The current study aims to develop a self-healing colloidal nanocomposite gel with combining different types of optimized organic and inorganic nanoparticles through mimicking the composition, structure and interactions between different components of bone tissue. Therefore, different types of organic (gelatin) and inorganic (calcium phosphate, bioactive glass and silica) nanoparticles will be synthesized and their surface properties (surface charge, surface chemistry and hydrophobicity) will be modified to obtain composite gels with improved self-healing properties.

2. MATERIALS

Gelatin types A and B, glycine ($\geq 99\%$), and tetraethyl orthosilicate (TEOS; 99.999% trace metals basis) were purchased from Sigma–Aldrich. Calcium hydroxide ($\text{Ca}(\text{OH})_2$, 98+%, extra pure), ammonium hydroxide (NH_4OH ; 25 wt% solution in water), sodium citrate tribasic dihydrate ($\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$), and Glutaraldehyde (GA, 25 wt% solution in water) were purchased from Acros Organics. Calcium nitrate tetrahydrate ($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$) was from Merck. Acetone and phosphoric acid (H_3PO_4 , 85%) were purchased from J.T.Baker. All the other reagents were analytical grade.

3. METHODS

A two-step desolvation method was used for fabrication of gelatin nanospheres as described elsewhere [1]. Bioactive silicate glass nanospheres with different calcium contents were synthesized via optimization of the Stöber method [2]. A precipitation method was used for preparation of calcium phosphate nanoparticles [3]. This wet chemical approach is based on a neutralization reaction between ortho-phosphoric acid and calcium hydroxide yielding apatitic nanoparticles, the aspect ratio and size of which can be finetuned by changing reaction parameters such as temperature as shown below:



4. RESULTS

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) techniques were used to evaluate the size and morphology of the synthesized nanoparticles. Figure 1 shows the SEM micrograph of positively charged gelatin nanospheres. As shown in this figure the particles were spherical and had the average diameter of about 160-170 nm.

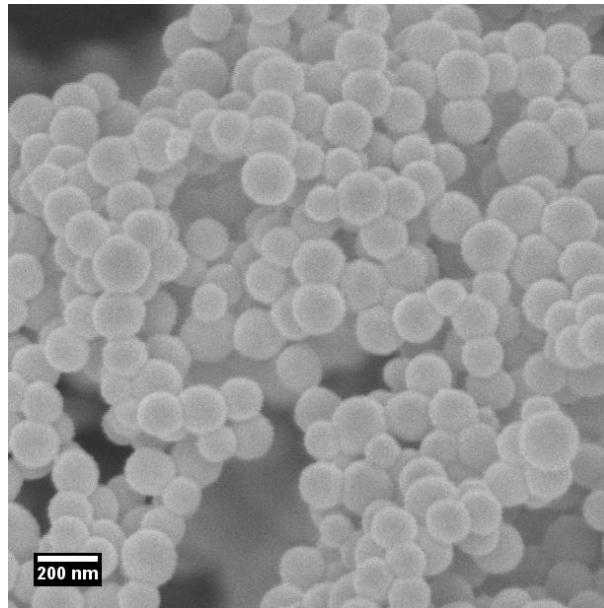


Figure 1: SEM micrograph of gelatin (type A) nanospheres.

In an attempt to explore the feasibility of using electrostatic and hydrophobic interactions between biopolymer nanoparticles, it was recently observed that colloidal gels made of oppositely charged gelatin nanospheres were surprisingly cohesive, elastic and self-healing [1] (as shown in Figure 2).

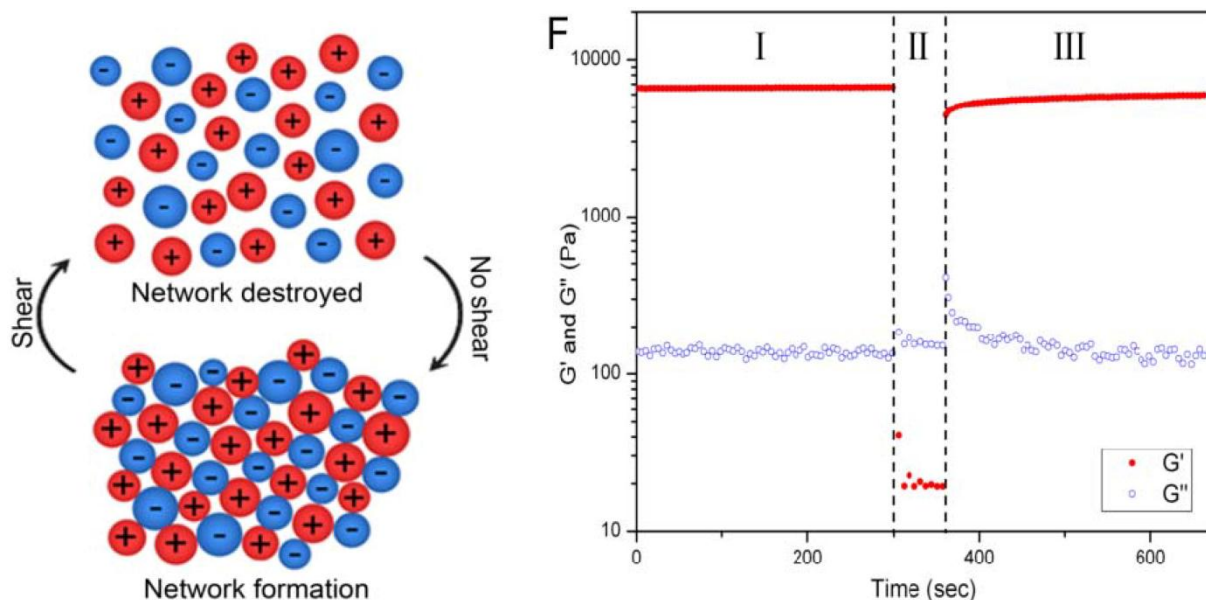


Figure 2: Fast and almost complete recovery of elasticity (G') of colloidal gels made of oppositely charged gelatin nanospheres upon gel network destruction (1000% strain) in phase II.

As shown in Figure 3, calcium phosphate and bioactive silicate glass nanoparticles were synthesized with needle and spherical shapes, respectively.

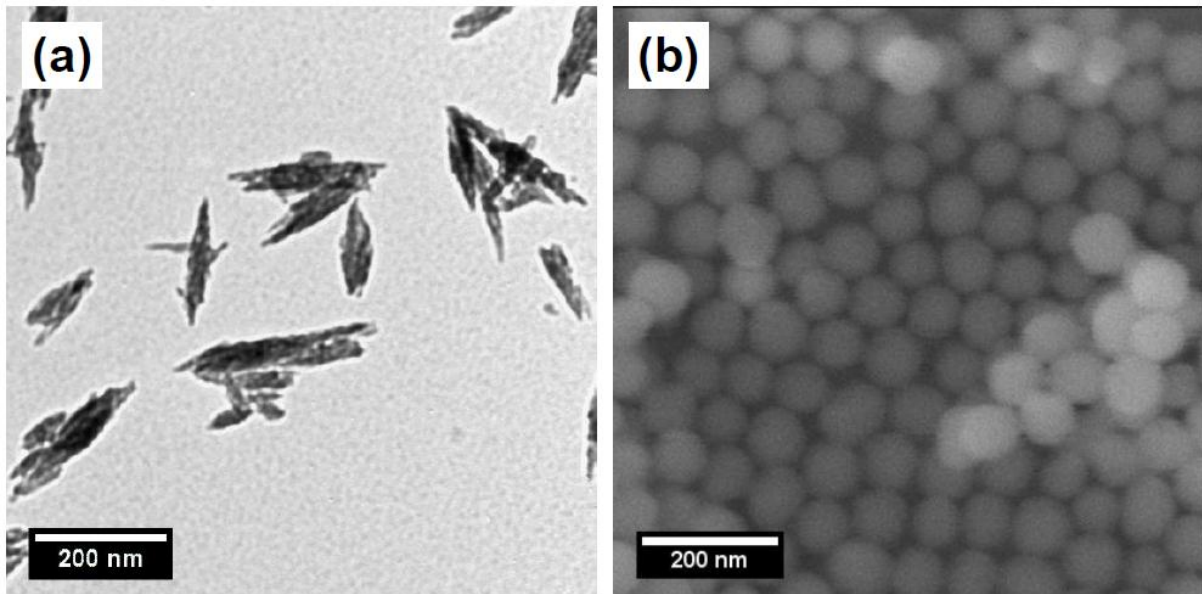


Figure 3: (a) TEM micrograph of calcium phosphate and (b) SEM micrograph of bioactive silicate glass nanoparticles.

Further studies will investigate the effects of these inorganic nanoparticles of different morphology and composition on self-healing properties of composite colloidal gels using techniques such as AFM and optical tweezers (at low solid content) and rheometry (at high solid content).

5. CONCLUSIONS

By combining organic and inorganic nanoparticles, self-healing colloidal gels will be developed in the current project based on optimization of reversible interactions between the nanoparticles. These nanocomposite gels will benefit from the flexibility and resilience of organic matter and hardness and rigidity of inorganic nanoparticles.

ACKNOWLEDGEMENTS

The authors thank AgentschapNL (IOP Self Healing Materials, Project no. SHM012014). The authors would like to thank Prof. Aldo R. Boccaccini for his helpful discussions on the synthesis of bioactive glass nanoparticles.

REFERENCES

- [1] H.A. Wang, M.B. Hansen, D.W.P.M. Lowik, J.C.M. van Hest, Y.B. Li, J.A. Jansen, and S.C.G. Leeuwenburgh, Oppositely Charged Gelatin Nanospheres as Building Blocks for Injectable and Biodegradable Gels, *Advanced Materials* 23 (2011) H119-H124.
- [2] W. Stöber, A. Fink, and E. Bohn, Controlled growth of monodisperse silica spheres in the micron size range, *Journal of Colloid and Interface Science* 26 (1968) 62-69.

[3] R. Kumar, K.H. Prakash, P. Cheang, and K.A. Khor, Temperature driven morphological changes of chemically precipitated hydroxyapatite nanoparticles, *Langmuir* 20 (2004) 5196-5200.