



Development of self-healing poly(γ -glutamic acid)/ chondroitin sulfate hydrogels with in situ mineralization ability



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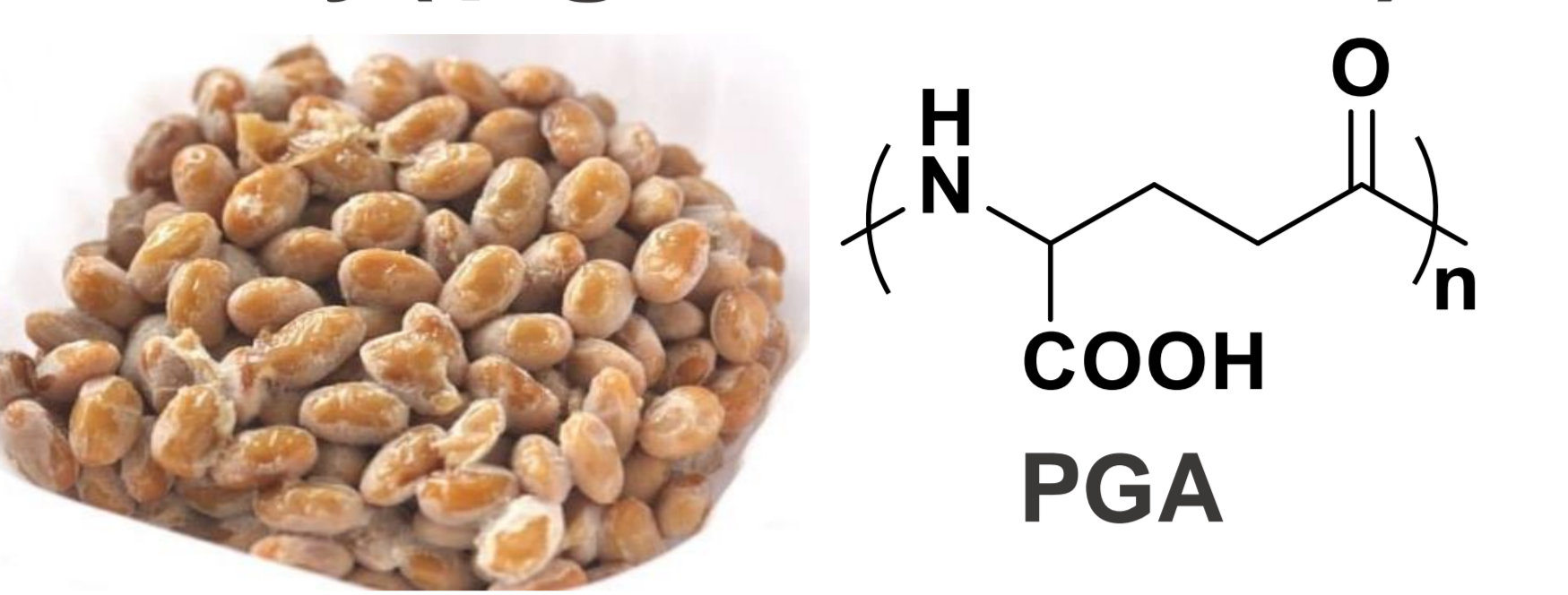
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Introduction

Poly(γ -glutamic acid)

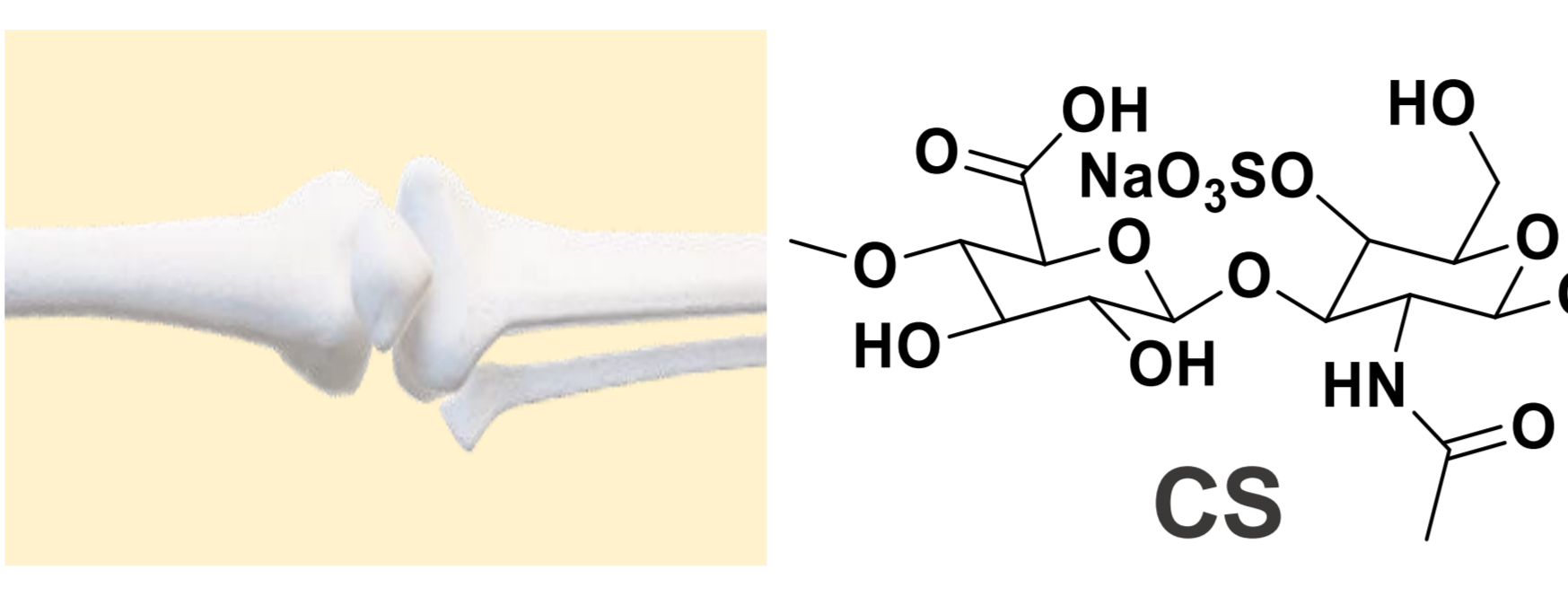


PGA

Park, S, et al. *Prog. Polym. Sci.* 2021, 113, 101341.
Sugino, A, et al. *J. Mater. Sci. Mater. Med.* 2008, 19, 2269–2274.

- Biodegradability
- Non-toxicity
- Excellent apatite-inducing ability

Chondroitin sulfate

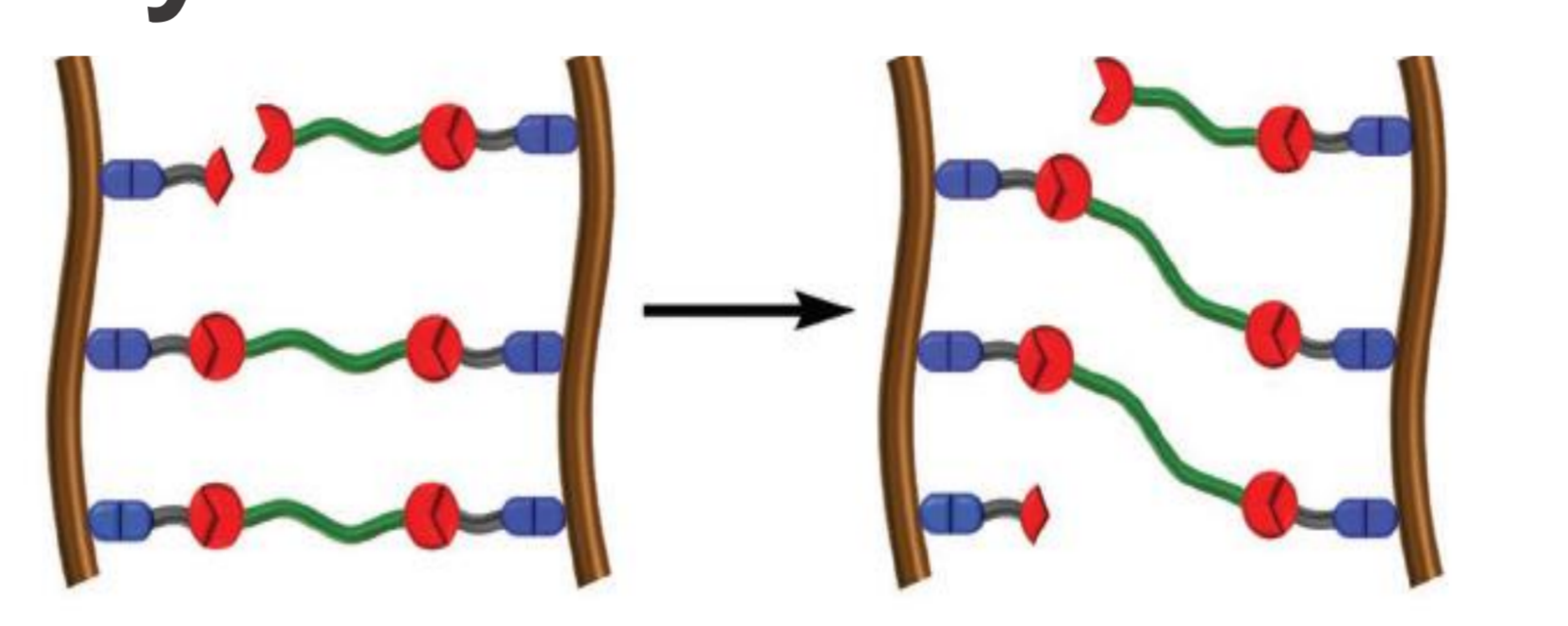


CS

Kim, H, et al. *ACS Appl. Mater. Interfaces* 2017, 9, 26, 21639–21650

- Anti-inflammatory activity
- Biocompatibility
- Good biomineralization

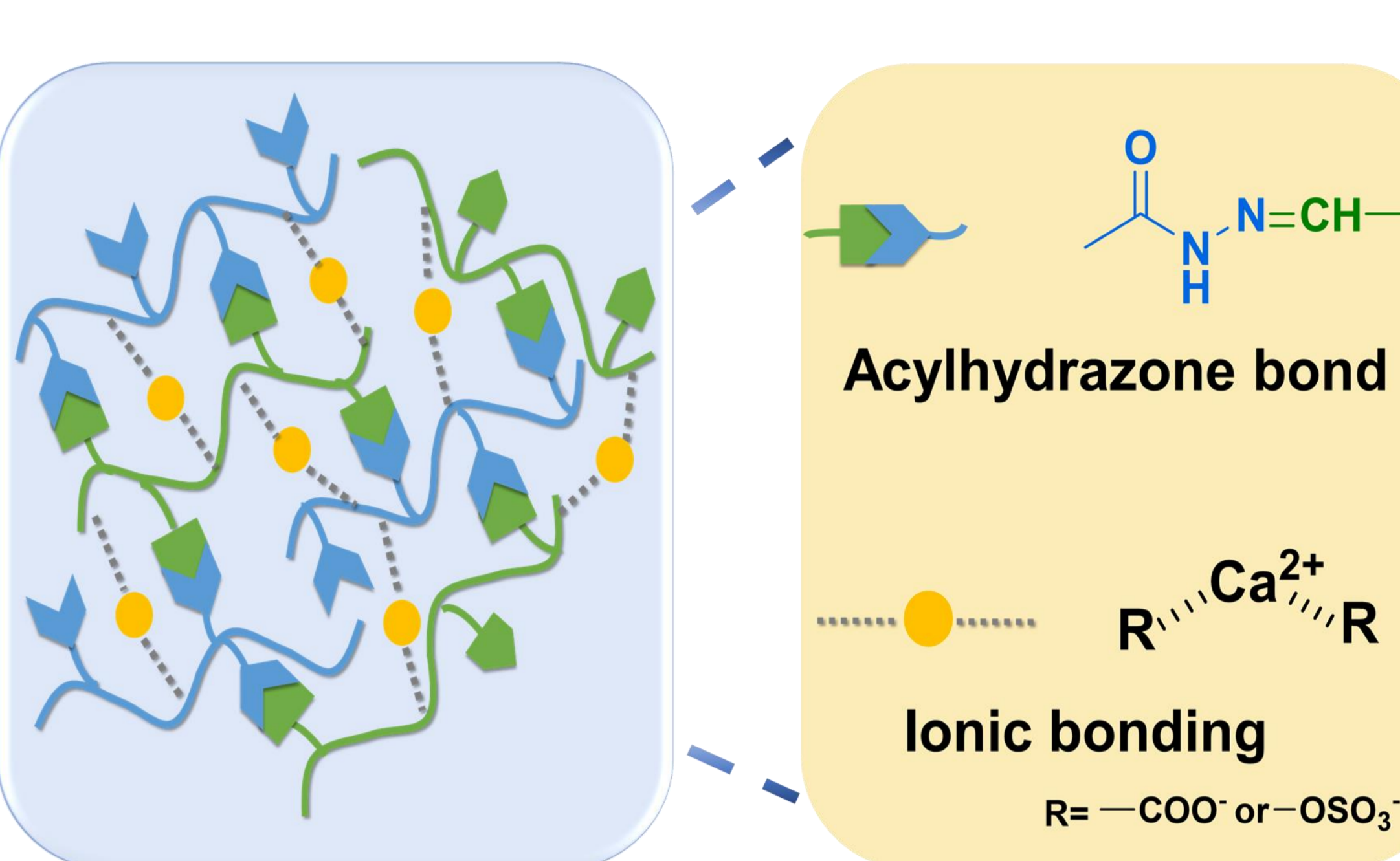
Dynamic covalent bond



Yang, X, et al. *Adv. Funct. Mater.* 2017, 27, 1703174.

- Injectability
- Self-healing ability
- Matchable dynamic properties

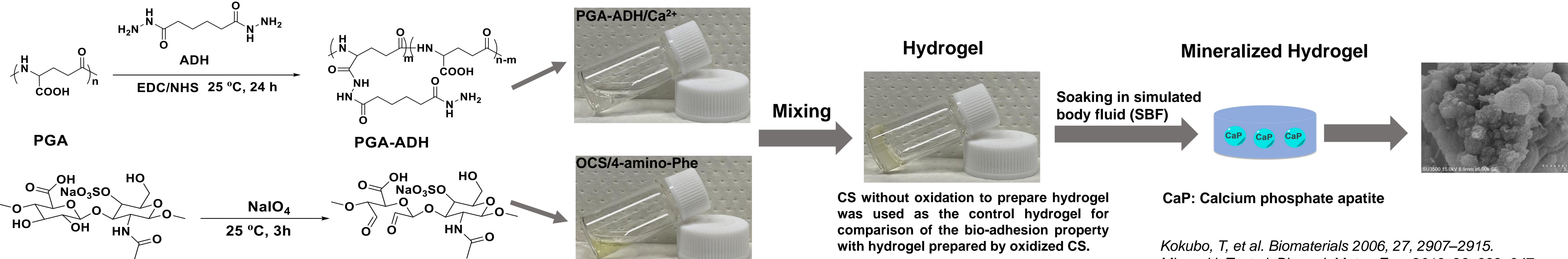
This study



Acylhydrazone bond

Ionic bonding
R—Ca²⁺—R
R = —COO⁻ or —OSO₃⁻

Experimental



PGA + **ADH** + **EDC/NHS** (25 °C, 24 h) → **PGA-ADH**

CS + **NaIO₄** (25 °C, 3 h) → **OCS**

PGA-ADH + **OCS** → **Hydrogel**

Hydrogel + **Soaking in simulated body fluid (SBF)** → **Mineralized Hydrogel**

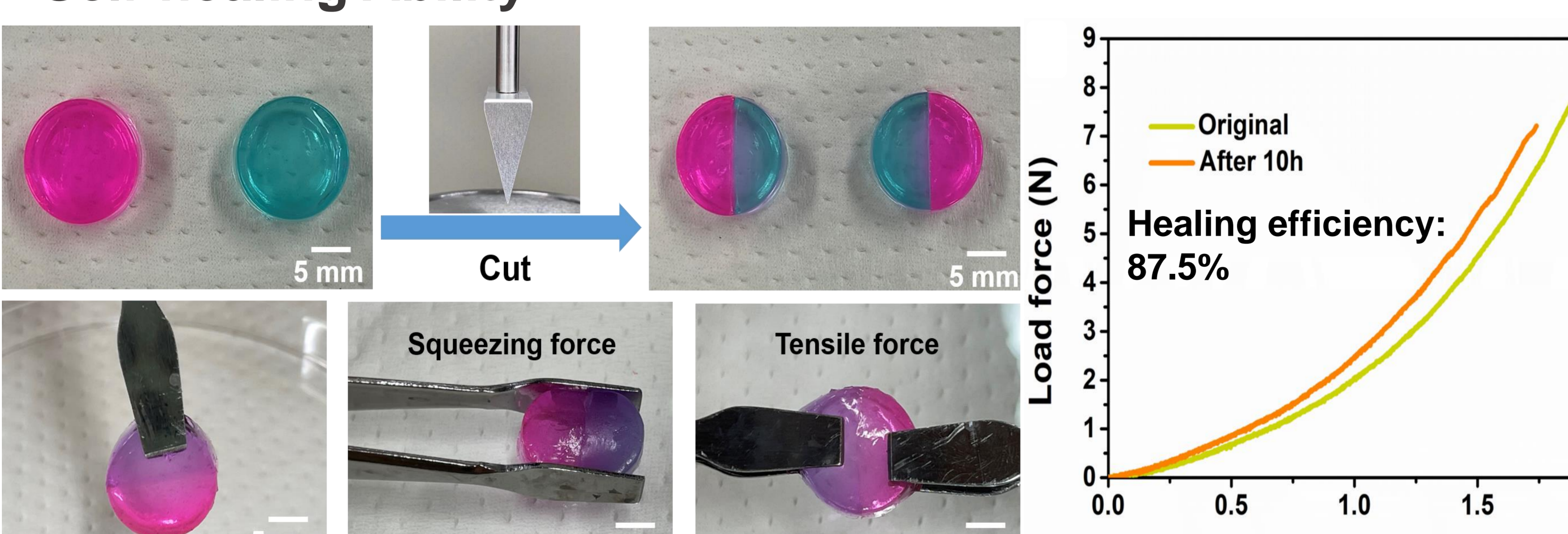
CaP: Calcium phosphate apatite

CS without oxidation to prepare hydrogel was used as the control hydrogel for comparison of the bio-adhesion property with hydrogel prepared by oxidized CS.

Kokubo, T, et al. *Biomaterials* 2006, 27, 2907–2915.
Miyazaki, T, et al. *Biomed. Mater. Eng.* 2013, 23, 339–347.

Results

Self-healing Ability

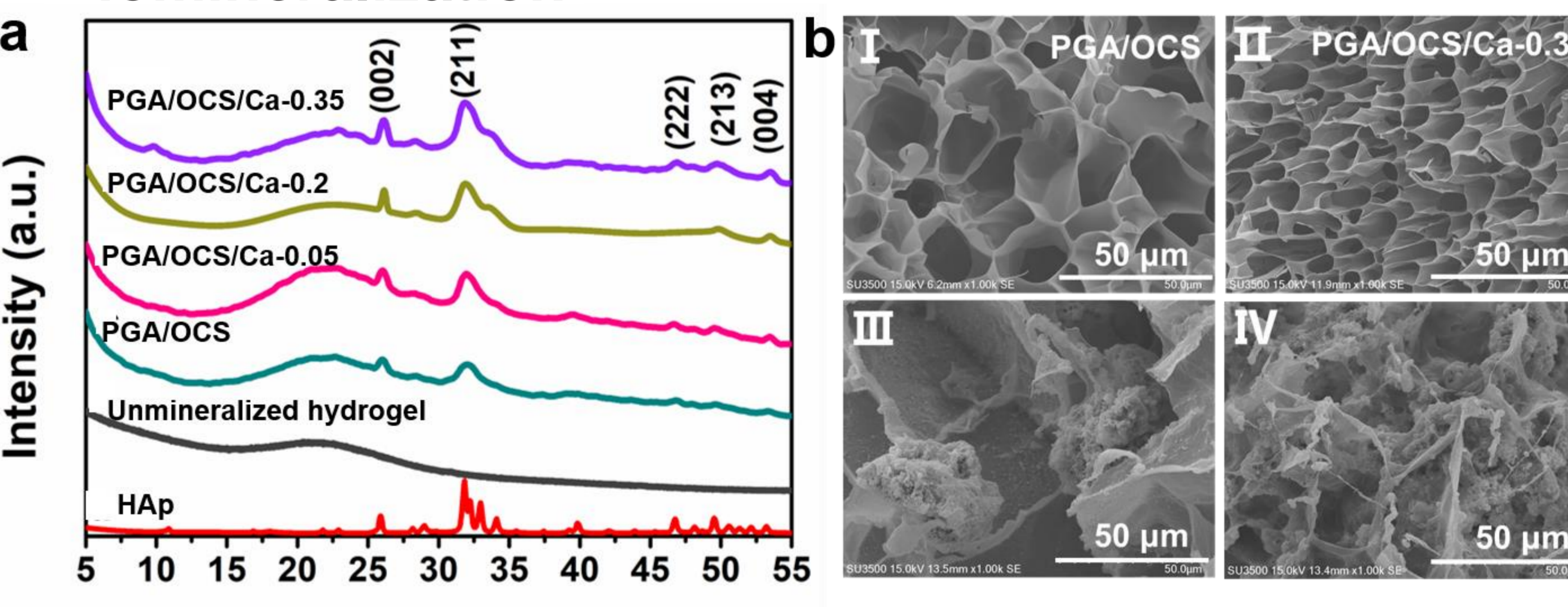


Healing efficiency: 87.5%

Load force (N) vs Displacement (mm)

— Original
— After 10h

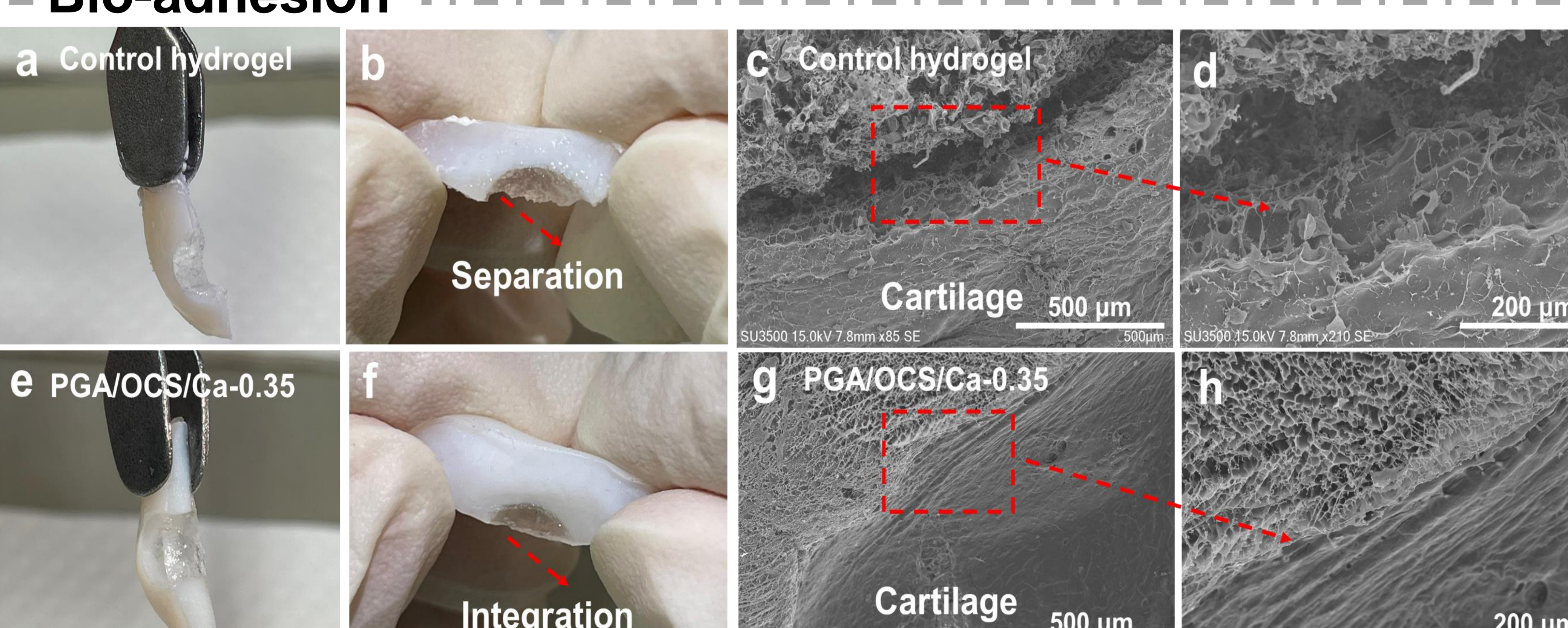
Biomineralization



a XRD patterns showing peaks for (002), (211), (222), (213), and (004) planes. Legend: PGA/OCS/Ca-0.35, PGA/OCS/Ca-0.2, PGA/OCS/Ca-0.05, PGA/OCS, Unmineralized hydrogel, HAp.

b SEM images of interiors of hydrogels (I, II, III, IV) showing porous structure.

Bio-adhesion



a Control hydrogel, **b** Separation, **c** Control hydrogel, **d** Cartilage (500 μ m, 200 μ m), **e** PGA/OCS/Ca-0.35, **f** Integration, **g** PGA/OCS/Ca-0.35, **h** Cartilage (500 μ m, 200 μ m).

Conclusion

- ✓ Hydrogels exhibited good self-healing capacity since the combination of acylhydrazone bonds and ionic bonding.
- ✓ The existence of Ca²⁺ ions promoted the formation of apatite in the hydrogels after immersing in SBF.
- ✓ Hydrogels displayed good tissue-adhesive property.

Acknowledgment: This work was supported by JSPS KAKENHI Grant No.20K15343.