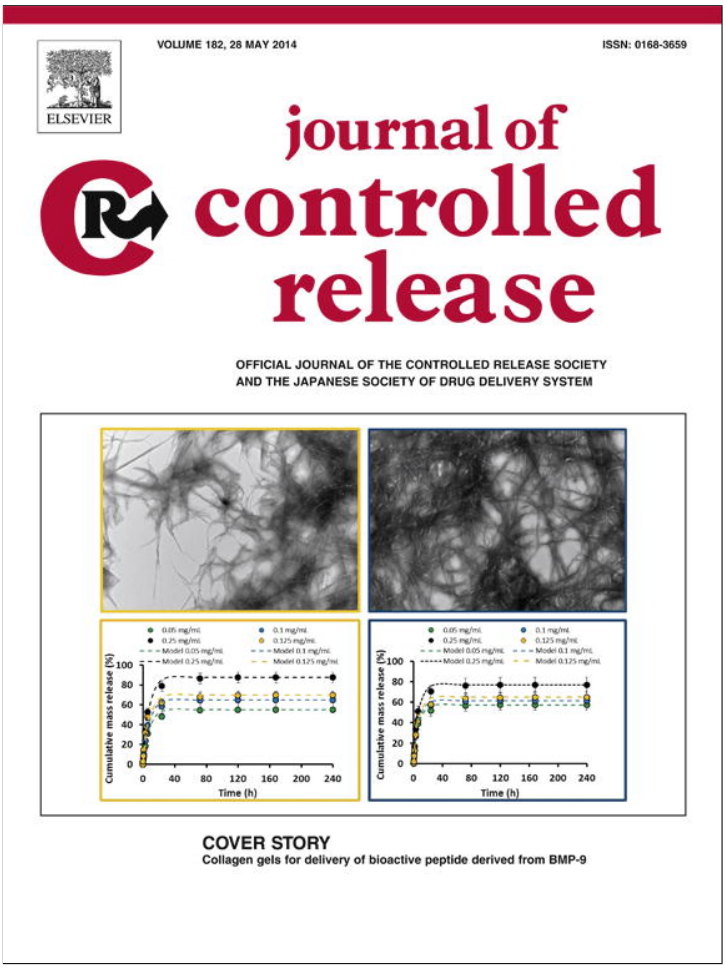

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Cover Story

Collagen gels for delivery of bioactive peptide derived from BMP-9

Type I collagen, the most abundant natural polymer in bones, is currently used in commercial growth factor delivery systems that release bone morphogenetic proteins (BMPs) like BMP-2 and BMP-7 as tibial fracture and spinal fusion treatments [1]. For example, the Infuse Bone Graft® system produces significantly faster spinal fusion in patients suffering from disk disease than autograft treatment, the gold standard treatment [1]. However, the *in vivo* half-life of BMPs is very short, and this requires the use of supra-physiological doses of growth factors. Such high doses can induce severe adverse effects, such as heterotopic ossification or osteoclast dysfunction [2]. Furthermore, BMPs are also very expensive, making the treatment extremely costly. Thus, peptides derived from the knuckle epitope of a BMP molecule (pBMP), *e.g.*, pBMP-9 derived from BMP-9, are potentially interesting alternatives [3]. Their effect *in vitro* is similar to that of the BMP and their substantially lower cost makes them a potential replacement for the current BMP release systems [4]. Nevertheless, very few studies have investigated the effects of various concentrations of collagen and initial peptide loads on the release of such a peptide.

The paper of Professor Faucheux and her team in this issue [5] presents interesting findings on the effect of the collagen content on the release behavior of pBMP-9. The Langmuir adsorption isotherms showed that both adsorption and the strength of the pBMP-9/collagen interactions were affected by increasing the collagen concentration. The transmission electron microscopy images revealed that increasing the concentration of type I collagen in hydrogels from 1.5 to 4.5 mg/mL enhanced the amount of fibers and their self-organization, leading to more entangled fiber mesh. The mathematical model proposed by the Faucheux team [5] was built as a multiphase phenomenon, where the pBMP-9 diffuses through the gel-like phase but can adsorb on, *i.e.*, interact with, the collagen fibers. The model has, in all cases, accurately represented the experimental data. The model also showed that diffusion was the dominant mass transfer mechanism inside the matrix with similar values among the collagen concentration range tested, which may be due to the high porosity of the hydrogels. Moreover, the mass transfer coefficient at the surface of the hydrogel varied most with the highest collagen concentration, which in turn impacted the pBMP-9 release. Further analysis also confirmed that both mass transfer resistance inside and at the surface of the releasing device have equal importance. The study by the Faucheux team indicates that both the effective diffusivity and the mass transfer coefficient are important in controlling the release of pBMP-9. It indicates that particular attention should be paid to the mass transfer coefficient assumption, since the perfect sink condition cannot always be assumed. The proposed mathematical framework is of particular interest since it can be applied to other porous systems where interactions may exist between the solute and the delivery system.

The study by Professor Faucheux and her colleagues is important to drug delivery for a few reasons. First, creating a bioactive peptide sequence derived from a protein makes it easier to design delivery systems and substantially lower the cost of treatment. This approach can be further extended into creating a small molecule drug having the same bioactivity. Second, peptides, as compared with proteins, are much more stable in various conditions, making the formulation development more flexible. Third, modeling the release of peptide drugs will be much easier than that of protein drugs which can undergo denaturation and unexpected behavior. In the end, the effectiveness of peptides or any drugs depends on control of the drug release kinetics. Long-term delivery with predesigned release kinetics of peptide drugs is still in its infancy stage, but the technology is improving rapidly, as the models like the one described by the Faucheux team improve our understanding on the drug release kinetics.

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Kinam Park
Purdue University
Departments of Biomedical Engineering and Pharmaceutics
West Lafayette, IN, USA
E-mail address: kpark@purdue.edu

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