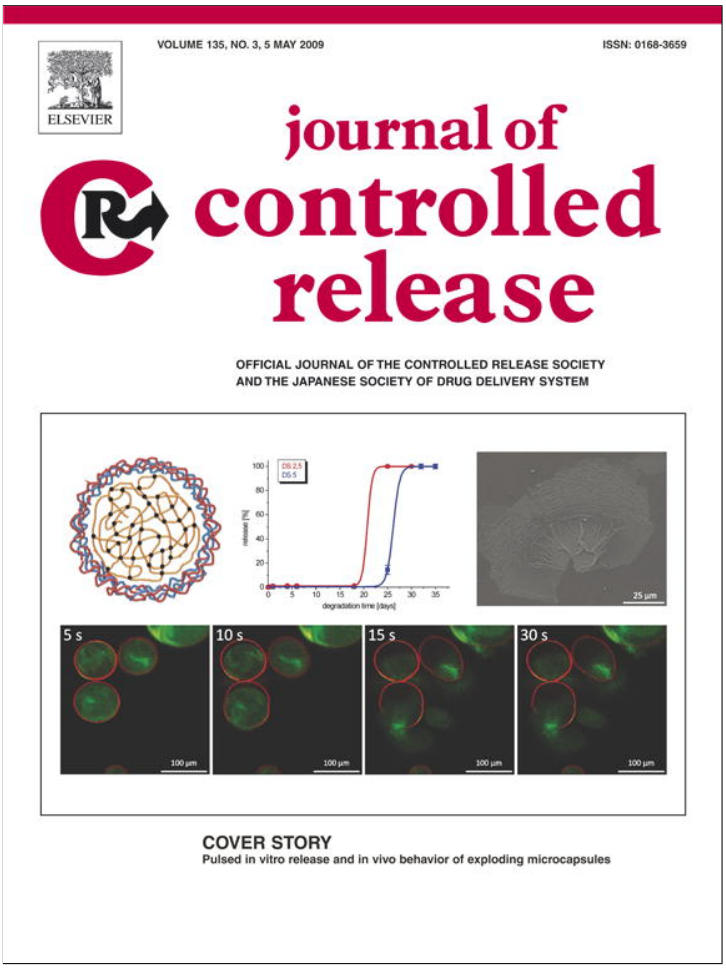

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Cover Story

Self-exploding microcapsules for pulsed drug delivery

The concept of pulsed drug delivery has been available since the introduction of osmosis-based drug delivery systems. An osmotic tablet without any orifice for drug release will eventually be ruptured by the osmotic pressure. Exact control of the rupture time, however, has been difficult. There has been a growing need for pulsatile delivery systems that can deliver their payload after predefined time intervals. Such systems will be ideal for delivery of vaccines that often requires multiple booster injections to generate sufficient immunity. A 'single shot' vaccine system would be especially well suited for Third World countries where full vaccination programs face huge logistic problems. Moreover, single-shot vaccination can improve patient compliance and reduce the overall healthcare expenses, resulting in considerable socio-economical benefits.

The paper by De Geest et al. in this issue [1] reports on pulsed drug release based on self-exploding microcapsules. These microcapsules consist of a biodegradable dextran-based microgel core surrounded by a semi-permeable membrane made of poly(L-arginine) and dextran sulfate. Upon degradation of the microgel core, the swelling pressure increases, as water is drawn inside the capsules by osmosis, until the tensile strength of the capsule membrane exceeds resulting in explosion of the capsule and release of the encapsulated material. In their previous papers the concept of self-exploding capsules was reported but several important issues still remained to be solved in order to obtain pulsed drug release at physiological conditions. In the present paper the authors report on fabrication of exploding capsules that are able to release their payload under physiological conditions in a pulsatile fashion *in vitro*.

Microcapsules having a mean diameter of 150 μm were used, instead of smaller (10 μm sized) microcapsules used in their previous papers, because rupturing larger capsules requires less pressure than for smaller capsules. Moreover, as a model drug 50 nm sized green fluorescent latex particles were used. The latex particles are expected to be too large to leak through the capsule's membrane prior to capsule explosion. For vaccination purposes, several antigens were preferably formulated in nanoparticles as this enhances both their uptake by antigen presenting cells as well as cross-presentation by antigen presenting cells. It was shown that the time point of explosion, and thus the release of the 50 nm green fluorescent latex beads, can be tailored by varying the cross-link density of the microgels. The time point at which the microcapsules explode and release of their payload is governed by the degradation rate of the microgel core. After having obtained pulsed release *in vitro*, the authors tested microcapsules *in vivo* to assess the tissue reaction after subcutaneous injection in mice. A moderate tissue inflammation was observed, which is normal upon injection of a foreign entity, and tissue sections of the injection spot revealed that after one month most of the capsules were observed to be broken. Another Cover Story in a previous issue featured smart nanogels that undergo volume phase transition upon temperature change [2]. Combining this smart nanogel property to the osmosis-based pulsatile delivery can lead to development of more advanced pulsatile delivery system, e.g., on-demand pulsed delivery in addition to predefined pulsed time intervals.

References

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[2] Y. Lee, S.Y. Park, C. Kim, T.G. Park, Thermally triggered intracellular explosion of volume transition nanogels for necrotic cell death, J. Control. Release 135 (2009) 89–95.

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