Constant Exposure of Poorly Soluble Drugs via Nanosuspension Release from Osmotic Pumps—An In Vitro/In Vivo Evaluation
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**Purpose**
To evaluate the *in vitro* and *in vivo* controlled release and biodistribution of drug nanosuspensions from osmotic pumps.

**Methods**
Different viscous nanosuspensions containing radiolabeled [125I]-dechloro-iodofenofibrate as model compound were produced via wet-milling on a stirred ball mill (Pulverisette 7, Fritsch GmbH, Idar-Oberstein, Germany) and released *in vitro* into a medium of 0.9% sodium chloride via osmotic pumps (Alzet® pump 1007, Durect Corp., Cupertino, USA). The optimized nanosuspension formulation was subsequently subcutaneously injected into female NMRI mice and distribution imaged via γ-scintigraphy (γ imager, biospace lab, Paris, France). Organ distribution studies of bolus injected nanosuspension and nanosuspension released from subcutaneously implanted osmotic pumps were additionally conducted via γ-scintillation (Berthold Technologies GmbH & Co. KG, Bad Wildbad, Germany).

**Results**
*In vitro* release of low viscous nanosuspension from osmotic Alzet® pumps exhibited unexpected burst release, whereas the adaption to a higher nanosuspension viscosity led to a zero-order delivery of nanoparticles. *In vivo* tracking of radiolabeled compound from bolus injected nanosuspension showed a decrease in distribution from the injection site, although a depot was formed subcutaneously. This was confirmed by the biodistribution experiments, where an exponential decrease of radiolabel concentration from directly injected nanosuspension could be observed throughout all investigated organs. The *in vitro* optimized nanosuspension released from subcutaneously implanted osmotic pumps in contrast showed a constant exposure of radiolabel up to a time duration of 168 h.

**Conclusion**
By *in vitro* optimization the feasibility of nanosuspension delivery from osmotic devices could be demonstrated. The delivery systems presents a valuable tool for constant drug exposure over prolonged duration in preclinical issues.