Conference abstract PNM17

Polyacrylic Acid-Protamine Nanoparticles for Scale-Up Experiments in a Microreactor

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Sci Pharm. 2010; 78: 687 doi:10.3797/scipharm.cespt.8.PNM17

Pharmaceutical drug formulations in the nanometer scale received significant interest during the last years as they provide the possibility to stabilize drugs and to transport them directly to their target. Biodegradable self-assembled nanoparticles consisting of protamine and oligonucleotides, so-called “proticles”, have already been successfully developed for different applications [1, 2]. However, the production could only be performed at the milliliter scale due to the sensibility with respect to parameter changes at larger volumes. For further investigations, such as in-vivo or clinical studies, it is essential to scale-up the production process to achieve larger amounts of proticles. As the introduction of a microreactor has been shown to have many advantages for the scale-up of nanoparticle formation processes, this approach is investigated for the production of proticles. The advantages of microreactors include the ability for continuous mixing of small volumes and the precise control of the operating parameters [3]. Because of the high costs of oligonucleotides, alternative nanoparticles comprising protamine and polyacrylic acid were developed for the first scale-up experiments. The characterization of these nanoparticles produced at the milliliter scale, included size and zeta potential measurements which were performed by Dynamic Light Scattering and Laser Doppler Electrophoresis. Protamine binding efficiency was determined by fluorimetry. After optimization of the process, particles of about 150 nm and a zeta potential of around 30 mV were produced exhibiting a suspension stability of at least 5 days. First experiments with a microreactor can now be started. This presentation will highlight some details of the microreactor, its advantages in the scale-up and the latest results concerning the nanoparticle production.
The project is supported by one-A engineering austria, Prager Elektronik and the Austrian NANO Initiative (Nano-HEALTH).

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