**Solvent Injection: A new approach for manufacturing lipid nanoparticles**

M. A. Schubert and C. C. Müller-Goymann

Institut für Pharmazeutische Technologie, Technische Universität Carolo-Wilhelmina zu Braunschweig, Mendelsohnstrasse 1, D-38106 Braunschweig

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**Introduction**

Nanoparticles based on solid lipids have been proposed as a promising alternative colloidal drug delivery system with respect to polymer nanoparticles and liposomes [1, 2]. The standard production method for the preparation of lipid nanodispersions based on solid lipids is high pressure homogenization [3]. Furthermore, lipid nanoparticles can be prepared by precipitation from microemulsions and emulsions containing organic solvents [4, 5]. As an alternative production method “solvent injection” commonly employed for manufacturing liposomes [6] and polymer nanoparticles [7] was investigated for its suitability for the preparation of lipid nanoparticles.

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**Experimental Methods**

**Materials**

- **Solid lipids**: softisan 100, softisan 142, softisan 154, witepsol H35 (CONDEA, D-Witten), cetyl palmitate (Caelo, D-Hilden).
- **Emulsifiers**: phospholipon 90G (Phospholipid, D-Köln), polysorbate 80 (Unigema, B-Everberg), poloxamer 188 (Synopharm, D-Barsbüttel).
- **Solvents**: acetone, ethanol, ethylacetate, methanol, isopropanol, 85% glycerol (Sigma-Aldrich, D-Seelze), bidistilled water.

**Preparation of lipid nanoparticles**

Lipid nanoparticles were prepared by a modified solvent injection technique. The lipids were dissolved in a water-miscible solvent (1-100 mg/ml) and then rapidly injected through an injection needle into a stirred (330 rpm) aqueous phase with or without surfactant. The resulting dispersion was then filtered with a paper filter in order to remove an excess of lipid.

**Particle size measurement**

The size distribution of the lipid nanoparticles was investigated by photon correlation spectroscopy (PCS) using a Zetasizer 3 (Malvern, D-Herrenberg). The different systems were investigated under an angle of 90° in a measuring cell AZ 0.40 x 12 mm (Braun, D-Melsungen). The different systems were investigated under an angle of 90° in a measuring cell AZ 0.40 x 12 mm (Braun, D-Melsungen). The size distribution of the lipid nanoparticles was investigated by photon correlation spectroscopy (PCS) using a Zetasizer 3 (Malvern, D-Herrenberg).

**Results And Discussion**

**Method screening**

For the preparation of lipid nanoparticles by solvent injection acetone, ethanol, isopropanol and methanol are suitable solvents in contrast to ethylacetate. With all studied solid lipids it is possible to prepare nanoparticles. The addition of polysorbate 80 or poloxamer 188 as emulsifier in the aqueous phase, respectively, or of phospholipon 90G in the solvent phase leads to smaller particles. The obtained particle size was depending on the preparation conditions between 80 and 300 nm.

**Assessment of the reproducibility**

After successful screening of the method “solvent injection” for nanoparticle preparation the reproducibility and reliability of the method was assessed (Fig. 1).

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**Conclusion**

“Solvent injection” is a straight forward method with no need of sophisticated equipment to manufacture lipid nanoparticles. The particle size can be influenced and controlled by variation of process parameters like injected solvent, lipid concentrations, injected amount and viscosity. One crucial parameter for the nanoparticle formation process seems to be the diffusion of the lipid-solvent phase in the aqueous phase.

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**References**