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## Flash nanoprecipitation as a simple route to produce smart polymeric drug delivery devices.

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Keywords: Nanoparticles; Caffeine; Flash NanoPrecipitation; Solvent Displacement; Drug delivery; PCL; CIJM; Drug Loading; Encapsulation Efficiency; Hydrophilic.

Flash nanoprecipitation (FNP) was proven to be a promising technology for the industrial production of drug loaded nanoparticles; however, only applications with hydrophobic compounds have been deeply studied up to now [1].

The presents research aims at demonstrating the possibility of encapsulating a strongly hydrophilic compound (caffeine) by FNP while keeping the control over product quality.

Caffeine loaded poly- $\epsilon$ -caprolactone nanoparticles were produced in a confined impinging jet mixer using acetone as solvent and water as antisolvent. Caffeine was dissolved alternately in acetone or in water to investigate the effect of the two different process configurations.

The nanoparticle quality was assessed in term of Loading Capacity (LC%), Encapsulation Efficiency (EE%) and *in vitro* release kinetics in order inquire the incorporation and release of the active substance.

The nanoparticle structure and dimension were analysed for the two process configurations by means of dynamic light scattering (DLS), scanning electron microscopy (SEM), and X-ray photo electron spectroscopy (XPS).

A preliminary study of the product shelf life was conducted both on the colloidal suspension and on the dried product by differential scanning calorimetry (DSC), infrared spectroscopy (FT-IR) and thermogravimetric analysis (TGA).

The produced nanoparticles were effective in terms of incorporating and slowly releasing caffeine.

A good control over the particles size was obtained by finely tuning the process parameters. The particle structure changed according the selected configuration, i.e. the active substance was more concentrated in the inner core of the particle when it dissolved in water and more adsorbed on the surface when dissolved in acetone, therefore the two structures displayed different release kinetics.

[1] Martínez Rivas CJ, Tarhini M, Badri W, Miladi K, Greige-Gerges, et al. Nanoprecipitation process: From encapsulation to drug delivery. *Int J Pharm.* 2017 Oct;532(1):66–81.