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(Article begins on next page)

OR-59

Production of PCL nanoparticles by Flash Nano Precipitation for controlled release of caffeine.

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Caffeine (CAF) is one of the most consumed drug worldwide due to its large application in food, pharmaceuticals, cosmetics and supplements; upon oral administration caffeine is cleared into the stomach in 20 minutes and absorbed into the blood within 1 hour [1].

Polycaprolactone (PCL) is biodegradable polymer extensively studied in drug delivery applications where long lasting releases are required [2].

Caffeine was encapsulated in PCL nanoparticles by exploiting the Flash nano-precipitation technique which is well known method to encapsulate hydrophobic drug [3], but not yet studied on hydrophilic active principles. The nanoparticles were produced in a confined impinging jet mixer by dissolving caffeine alternatively in the solvent (acetone or in the antisolvent (water).

The effect of the process parameters on the mean particle diameter and zeta potential of the nanoparticles was investigated by Dynamic Light Scattering. A novel methodology to accurately quantify drug Loading Capacity (LC) and Encapsulation Efficiency was studied and implemented.

The in vitro release kinetic was assessed by dynamic dialysis method.

Nanoparticle with average diameter ranging from 250 to 500 nm were successfully produced, the mean size was correlated to the flow rate.

LC and EE were assessed in the range of 10-45% and 5-25% respectively.

The release test showed a 1st order kinetic with a peak of caffeine in blood mimicking solution delayed to 6 hours.

[1] P. Nawrot, S. Jordan, J. Eastwood, J. Rotstein, A. Hugenholtz, and M. Feeley, *Food Addit. Contam.* **20** (2003) 1–30.

[2] V.R. Sinha, K. Bansal, R. Kaushik, R. Kumria, and A. Trehan, an overview, *Int. J. Pharm.* **278** (2004) 1–23.

[3] A. Ferri, N. Kumari, R. Peila, and A.A. Barresi, *Can. J. Chem. Eng.* **95** (2017) 1690-1706.