Ribavirin entrapment into PLGA NPs by using a novel microfluidic approach

Marco Bramosanti[1*], Laura Chronopoulou[1], Fabiana Grillo[1], Alessio Valletta[2], Livia Donati[2], Gabriella Pasqua[2], Cleofe Palocci[1]

[1]*Department of Chemistry, Sapienza University of Rome, Piazzale A. Moro 5, 00185 Rome, Italy*
[2]*Department of Environmental Biology, Sapienza University of Rome, Piazzale A. Moro 5, 00185 Rome, Italy*
**e-mail: marco.bramosanti@uniroma1.it*

The chemical treatment called "chemotherapy of plants" consists in the "in vivo" administration of substances capable of interfering with the viral replication. The current availability of synthetic molecules with a high chemotherapy index, i.e. with a high ratio between the maximum concentration tolerated and the minimum effective, together with the possibility to further widen the therapeutic window by the use of appropriate nanocarriers, seems to open on the application level of a novel chemical approach to treat plant viral infections. Ribavirin, for example, is a synthetic water-soluble nucleoside that possesses broad spectrum activity against a variety of DNA and RNA plant viruses. As well known, water-soluble drugs are generally difficult to encapsulate in solid particles[1]. Chemical modification of these drugs, such as esterification, may increase their encapsulation efficiency, but may also decrease bioactivity.

In this work we have synthesized stable solid monodispersed PLGA (poly-D,L-lactic-*co*-glycolic acid) NPs with diameters ranging from 50 – 200 nm containing ribavirin by using a microfluidic reactor with a flow-focusing geometry. In the flow-focusing-based microdevice the dispersed organic phase containing PLGA (i.e., acetonitrile) is continuously focused by the continuous phase (i.e.,ribavirin in acetate buffer pH 5.5) using 2 syringe pumps (Fig. 1 left). Previous works carried out in our labs [2] showed an improvement of drugs loading efficiency when using a microfluidic approach in comparison with traditional nanoprecipitation methods for nanoencapsulation. On this basis we optimized Ribavirin loading within PLGA NPs by investigating the influence of different operating conditions, such as polymer molecular weight and concentration, flow rate ratio, τmix, microreactor-focusing channel diameters and length, on nanoparticles' size and morphology and drug loading. NPs' characterization was performed by Dynamic light scattering (DLS) measurements (size and Z-potential), and by scanning electron microscopy (SEM). The determination of free ribavirin was carried out spectrophotometrically. Synthesized NPs, although the study is still preliminary, showed significant drug loading and entrapment efficiency[3].

Fig. 1 (left) CFM reactor system used for the synthesis of PLGA NPs. One outlet(c) connected by a cross junction (d), creating a hydrodynamic flowfocusing with a central stream (b) and 2 side streams (a and a').(r) can be varied by altering the Volumetric flow rates of the 3 inlets or the internal dimensions of the mixing channel. (right) SEM micrograph of PLGA ribavirin loaded NPs. Scale bar 2 micron

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