Characterization of polymer based nanopharmaceuticals by Asymmetrical Flow Field Flow Fractionation

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The rapid development of nanotechnologies strongly impacts advancement of the pharmaceutical industry. Polymeric particles have been extensively studied in the field of drug delivery. In order to be effective as drug delivery systems, nanoparticles (NPs) must have some specific features since their physical properties such as size, shape and optical properties strongly influence their therapeutical action [1]. The European Commission recommends the development of analytical methods for the quality control and characterization of NPs to avoid limitation of the implementation of nanotechnology to the real application. Since the definition of "size" (e.g. geometrical, hydrodynamic or optical radius) is method-dependent, the development of only one analytical technique to fully characterize complex NPs samples is not sufficient. Thus, it is often better to compare results obtained by different techniques even if data interpretation is not always easy.

In that objective, we develop different approaches to characterize nanopharmaceuticals based on different principles: DLS (Dynamic Light Scattering) for hydrodynamic diameter determination and A4F (Asymmetrical Flow Field Flow Fractionation) hyphenated to UV (Ultraviolet-Visible), MALLS (Multi-Angle Laser Light Scattering) and RI (Refractometer) detectors. Contrary to DLS, A4F-UV-MALLS-RI is not limited by disperse samples and provides a wide number of information but it requires a high level of analytical development and expertise. A4F is a device based on size separation and allows separation and isolation of NPs while maintaining native conditions for further characterization when associated with online or offline detectors. It offers the possibility to analyze a wide variety of macromolecules and particles ranging from the nanometer to the micrometer with a high resolution [2]. MALLS hyphenated with RI and UV as concentration detectors can give information about the molar mass, polydispersity, gyration radius, size distribution, conformation, PEGylation degree and encapsulation efficiency of NPs.

As a partner of NanoPilot H2020 European project, UT2A is responsible of the characterization of three different nanopharmaceuticals produced in the frame of this project. A4F-UV-MALLS-RI is used for the characterization of materials thoughout the synthesis process of nanopharmaceutical, from the control of raw materials to the final product.

First studies were focused on the determination of the molar mass and the polydispersity of raw materials as they are considered critical parameters for the formulation. This step was necessary to validate analytical methodologies and defined the most appropriate raw materials for further synthesis. In process formulation analysis, the presence of NPs with a size around 100nm was found but other compounds that should normally form NPs are also present. Results obtained allow us to propose A4F to control the efficiency and to optimize the process according to GMPs.

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References

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