From Nanotechnology to Medicinal Products: the Dosage Form as the Bridge to Clinical Translation

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Research in pharmaceutical technology can have a significant impact on improving the performance of medicinal products containing both new and old drug substances. The same Active Pharmaceutical Ingredient (API) can, in fact, be formulated into innovative pharmaceutical dosage forms and/or administered via novel routes. Such innovations, from both technological and biopharmaceutical perspectives, may improve clinical outcomes by modifying pharmacokinetics and/or biodistribution, thereby enhancing safety, efficacy, and patient adherence to therapy. Technological advancements, however, may require the modification or adaptation of existing legislative acts and regulatory guidelines to preserve the high standards of public health protection ensured by pharmaceutical legislation. At the same time, guidelines are issued on a risk–benefit basis and it is responsibility of pharmaceutical researchers to provide strong evidence and identify Critical Quality Attributes (CQAs). When dealing with nanovectors, the level of complexity increases since they require a further step to be administered via the selected route: the dosage form. For this reason, it is essential to elucidate the possible interconnections which can influence the biopharmaceutical performance, define CQAs and establish a set of assays to assist the development and the manufacturing phase. This approach would accelerate the clinical translation of nanovectors.
With this perspective, our research interest has been devoted to correlate biopharmaceutical properties of drug delivery systems to efficacy and safety also with the aim to promote assays for quality control purposes. This can be traced back to the study of (trans)dermal patches, in particular in the attempt to investigate the influence of nanosystems on adhesive properties [1] and *in vitro* skin permeation studies [2]. The expertise gained led to the design of mucoadhesive dosage forms, which are enabled to adhere to a biological tissue, and, subsequently, orodispersible films (ODF) produced with the same technologies. These latter are of growing interest in the shift towards a patient-centric design of pharmaceutical forms, not only because ODF address the unmet needs of special populations of patients, but also they can incorporate micro-and nanosystems allowing a fine tune-up of the drug release [3]. In addition, an in-depth investigation on the development of long-acting injectable (LAI) products has been conducted, dealing with both formulation aspects, including terminal sterilization, and the biopharmaceutical properties, as required by the Regulatory Agencies to develop new medicinal products or generic equivalents. The first of these activities led to the design of antioxidants grafted polymers which resulted stable upon irradiation and improved the encapsulation of hydrophilic drugs in nanoparticles [4]. The second allowed the definition of biorelevant media suitable to assess the in vitro drug release after injection in subcutaneous tissue or local administration [5]. Drawing on the knowledge acquired from these studies, our work has progressively expanded towards nanotechnology, with a focus on the design of nanosystems and the post-marketed safety based on real world data [6].

References

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