Preparation of biocompatible polymer-based drug delivery systems by continuous flow technique

Norbert Varga[a,b], László Seres[a,b], Kata Panna Kókai[c], Ádám Juhász[a,b] and Edit Csapó[a,b]

[a] *MTA-SZTE Lendület "Momentum" Noble Metal Nanostructures Research Group, University of Szeged, H-6720 Rerrich B. sqr. 1, Szeged, Hungary*

[b] *Interdisciplinary Excellence Center, Department of Physical Chemistry and Materials Science, University of Szeged, H-6720 Rerrich B. sqr. 1, Szeged, Hungary*

[c] *Institute of Pharmaceutical Technology and Regulatory Affairs, Faculty of Pharmacy, University of Szeged, H-6720 Szeged, Hungary*

vargano@chem.u-szeged.hu

Nowadays, the polymer-based nanostructured drug carriers play a key role in the field of nanomedicine [1]. By using them, we can prolong and increase the efficacy of the drugs. Due to the excellent biocompatibility and good material properties, the poly(lactide-co-glycolide) (PLGA), poly(lactide) (PLA), or polycaprolactone (PCL) polymers are some of the most popularly used biopolymers in the development of new types of colloidal drug delivery systems. The importance of these polymers are also shown by the fact that many types of batch-based techniques were developed for the formation of the drug delivery systems, such as nanoprecipitation, double emulsion, etc., where the properties of the particles can be tuned by the preparation conditions. However, these methods are mainly applicable to the production of smaller sample volumes, and they can only be used in stages to produce a higher amount of particles. Various microfluidic devices are ideally suited for eliminating these issues, where more controllable preparation processes can be feasible in contrast to the batch-based methods [2]. With these techniques, the properties of the particles can be controlled by the flow conditions (flow rate, relative flow rate, type of the mixer cells (active or passive), etc.); thus, we can optimize the carrier systems for the drugs. Taking these into account, our aim is to prepare PCl-based drug-containing nanoparticles (NPs) by microfluidic systems and to determine the effect of the synthesis parameters (e.g., flow conditions, concentration, quality of stabilizing agents) on the size, polydispersity, encapsulation efficiency, and structure of the NPs. In order to fully characterize the particles, DSC, FT-IR spectroscopy, DLS, TEM, and UV-Vis measurements were used. During the synthesis of the PCl NPs, it has been proved that the hydrodynamic diameter and the size distribution of the particles can be controlled with the changing of flow rate, where, depending on the flow parameters, 210–300 nm particle size can be achieved. Based on the UV-Vis and DSC studies, 50–60% encapsulation efficiency (EE) and 18–25% drug loading (DL) can be achieved using vitamin D3 as a model drug. Dissolution properties of D3 were also determined in physiological conditions (pH = 7.4) and model gastric juice medium (pH = 1.5), where the results pointed out that release processes are greatly controlled by the type of stabilizers. The dissolution curves were fitted by different kinetic models, and the diffusion-controlled features of the encapsulated model drug were obtained at the 0-360 min interval.

Keywords:
colloidal carriers, biocompatible polymers, polycaprolactone, continuous flow system, drug formulation

References:

[1] J. Jacob, J.T. Haponiuk, S. Thomas, S. Gopi, Biopolymer based nanomaterials in drug delivery systems: a review, Mater. Today Chem., 9, (2018), 43-55, 10.1016/j.mtchem.2018.05.002
[2] M. Mubashar Saeed, E. Carthy, N. Dunne, D. Kinahan, Advances in nanoparticle synthesis assisted by microfluidics, Lab on a Chip, 25, (2025), 3060–3093. https://doi.org/10.1039/D5LC00194C

Acknowledgements:
Project no TKP2021-EGA-32 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme. E. Csapó thanks the financial support of the "Momentum" Program of the Hungarian Academy of Sciences (LP2021–5). N. Varga thanks the financial support of Mecenatúra Scholarship (MEC_R_26 – 154655).