Application of 3D printing techniques dynamically expands in various areas and these techniques have been also applied in pharmaceutical sciences. Researchers have been working on using these techniques for manufacturing pharmaceutical products. In 2016, the first commercial product manufactured by 3D printing (immediate release Leviteracetam - Spritam) has been officially registered by Food and Drug Administration (FDA). 3D printing techniques are currently regarded as the techniques, which can revolutionize design, manufacturing and delivery of active substance during the coming decades, particularly manufacturing of personalized dosage forms.

There are strong premises that pharmaceutical and physicochemical properties of modified release oral dosage forms manufactured using 3D printing differ from those obtained using standard tableting methods. Following issues related to 3D printing in pharmaceutical technology remain untouched:

- Mass (water) transport inside 3D printed matrix under hydration;
- Influence of geometry and structure on mass transport and in consequence on drug release;
- Scaling rules for printed, personalized therapy aimed, matrix dosage forms;
- Safety and durability of 3D printed dosage forms.

The most important question to answer arises: is it possible to develop fundamentals of 3D printing based manufacturing technology of modified release, personalized (according to patient needs) dosage forms with predictable dissolution characteristics.

Scientific hypotheses which serve as a base of the proposed project are:

- knowledge about and quantification of physicochemical phenomena inside the hydrated matrix can aid designing the 3D printed dosage forms
- at initially fixed composition of the printing material (filament with active substance and fillers) the possibility exists to design internal structure and geometry as well as setup printing parameters (parameters easy to setup for 3D printing) the way to be able to adapt their properties to patient requirements in terms of right dose depending of the changing physiology (geriatrics), patient weight and ontogeny (pediatrics), metabolism and ideally individualized pharmacological kinetics parameters, i.e. to fulfill personalized medicine demands.

3D printing gives flexibility in defining internal and external structure of the polymeric matrix system. The main goal of the project will be the characterization of such systems with designed geometry and internal structure and assessment of their impact on pharmaceutical and physicochemical properties during hydration, particularly on active substance dissolution at simulated *in vivo* conditions (biorelevant dissolution).

As a result of the project we expect to develop basis for the rational design methodology for personalized oral modified release dosage form manufactured using 3D printing methods. Design method will integrate several analytical/physical methods applied *in vitro* both on dry and on partially hydrated samples, and data analysis tools based on artificial intelligence. The research will be focused on properties important for system behavior in the *in vivo* conditions. The physiological conditions of the system, understood as the human body, will be mimicked with the use of the validated physiologically based pharmacokinetic (PBPK) model.

As a model active pharmaceutical ingredient (API) ropinirole hydrochloride has been chosen. This drug substance used in Parkinson's disease treatment is applied in the wide range of doses from 0.75 mg to 24 mg per day and dosage regimen can change dynamically depending on the patient state. Currently, pharmaceutical products containing ropinirole are available as tablets with doses of 0.25, 0.5, 1.0, 2.0 and 5.0 mg. Actual dose should be combined using (a large) number of unit doses. It increases risk of mistake and decreases patient safety and compliance.

The work-plan can be shortly described as: composition – preformulation – matrix structure/geometry – mass transport – pharmaceutical effect – PBPK simulated *in vivo* effect.

The aims of the proposed research are:

(1) to understand complex processes of hydration and drug dissolution from 3D printed dosage forms manufactured by fused deposition modeling (FDM);

(2) to develop fundamentals of modern methodology for personalizing modified release matrices by adjusting internal structure and shape of dosage form as well as adjusting 3D printing process parameters.

(3) Establishing PBPK model for ropinirol, which will be utilizing the literature available absorption and metabolism data and results of physicochemical and pharmaceutical analyses (including dissolution) for the patient specific pharmacokinetics prediction.

The project has a potential to revolutionize the approach to design and manufacturing of the pharmaceutical oral modified release drug products for personalized therapy. It will establish methodological scaffold allowing for the individualized therapy planning. The results of the project will be important not only for 3D printing dosage forms but also for those manufactured with currently used industrial manufacturing methods.