Superparamagnetic iron oxide-based nanoparticles (SPIONs) exhibit unique physicochemical properties, making them an attractive material to be used in many biomedical applications, including use as a contrast agent in magnetic resonance imaging (MRI). These particles are mainly based on the Fe_3O_4 and/or Fe_2O_3 particles sized below 12 nm that can be easily doped and/or modified onto surface with biologically active compounds to interact with biological membranes. An interesting approach is the use of MRI to track distribution of therapeutic agent after administration in the real time.

Traditional method of evaluating drug distribution is measurement of plasma drug concentrations which do not reflect the local concentration of therapeutic agents delivered to the target areas. Real-time monitoring of therapeutic outcomes can help to track and tailor drug doses. One of the strategies to achieve this goal is via the use of theranostics. This term refers to the integration of imaging and therapy in one carrier. Its use with antimicrobial drugs may be of great importance in increasing the therapy effectiveness and reducing the development of drug resistance.

Active agents, which will be used during the project, are antifungal drugs: voriconazole and isavuconazole. These substances were chosen because invasive fungal infections are considered one of the most serious conditions. Currently, over 300 million people are suffering serious fungal infections and the annual mortality is more than 1.6 million worldwide. Pulmonary aspergillosis (caused by *Aspergillus spp*.) has raised vital concerns in clinical healthcare, as it mainly affects people with weak immune systems (e.g., infected with HIV/AIDS, transplant patients).

Pulmonary fungal infections are difficult to treat as the fungal spores penetrate deep into the small airways. Current therapy involves treatment with antifungal azoles, which are predominantly dosed either orally or intravenously (IV). Such a systemic administration is associated with poor lung distribution of the drug and failure to keep effective drug level at the site of infection. Antifungals need to be administered in high doses, which increases the risk of systemic toxicity and is responsible for the occurrence of serious side effects. Hence, pulmonary route of administration offers targeted drug delivery to the deep lung and reduction of systemic drug exposure.

Therefore, an interesting alternative to oral or IV administration of active agents, which are targeted to the lung, is inhalation. This makes it possible to achieve a therapeutic concentration of active substance in the lung using lower dose compared to general administration, thereby providing increasing the therapy efficacy and reducing the peripheral side effects. In addition, the use of drug carriers allows for sustained and controlled drug release.

The therapeutic effect after inhalation is not solely dependent on the drug dose, but also on the region of the lung deposition. Therefore, there is an interest in the possibility of monitoring the distribution of the drug administered by inhalation, allowing to observe the progress of the disease and the effects of therapy. Thanks to incorporating SPIONs into the drug carrier structure, it is possible to monitor drug delivery with MRI and assess the actual drug distribution in the lungs, as well as quantify the local drug concentration.

The aim of the project is to investigate the possibility of using SPIONs as contrast agent, enabling imaging of drug deposition in the lung by MRI, in inhaled theranostic dry powder formulation containing antifungals: voriconazole and isavuconazole, prepared by spray drying.

During the project SPIONs will be synthesized and then inhaled formulation containing antifungals and SPIONs will be prepared via spray drying. Further investigation will concern inhaled theranostic particles deposition in the lungs, particles size and drug release. Biological *in vitro* tests will be carried out on human lung epithelial carcinoma cell line A549, which is a model cell line to test substances administered by inhalation, the macrophage line and Calu-3 line. The results will be used to assess the possibility of contact SPIONs and dry powder formulation with the pulmonary epithelium. To investigate SPIONs imaging ability MRI technique and model of lung tissue from cellulose sponge will be used.

The expected results of the project are:

1. Establishing the relationship between the composition and ratio between components of nanocarriers, drug release rate, and the effectiveness of the nanocarriers on the delivery of the antifungal drugs as well as diagnostics using MRI.
2. Determination of the concentration range in which the use of SPIONs is safe, and the MR imaging capabilities are sufficient to assess the distribution of the drug in the lungs
3. Preparation and characteristic of inhaled theranostic dry powder containing SPIONs and antifungals