Inhalable microcarriers as drug delivery systems to the lungs in a dry powder formulations

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Diseases of lower respiratory airways such us acute and chronic infections, lung cancer, SARS-COV2 are one the most frequent causes of death worldwide as they can significantly compromise gas exchange in the alveoli. Such diseases are usually treated by systemic therapy, although lungs can be directly targeted through airways. Thus, by using inhalable formulations it is possible to obtain higher concentration of active pharmaceutical ingredient directly at their action site and reduce their amount distributed systemically. The two main benefits of inhalable drug delivery systems are: reduced side effects thanks to lower doses administered than via typical enteral or other parenteral routs, and in the case of antibiotics – lower chance to build up antibiotic resistance. To achieve the most effective therapy fabricated powders must have: appropriate size (1 – 5 μm in diameter), uniform size distribution, required aerodynamic properties to be deposited in the bronchiole/alveoli region, sufficient drug loading and release kinetics.

In our group we are working on lipid and polymer microparticles to be used as inhalable dry powder formulations. So far we have developed novel, inhalable stimuli-sensitive drug carriers that are intended to enhance the efficacy of lung cancer therapy through guided accumulation directly at the tumour site and controlled drug delivery triggered by alternating magnetic field resulting in local increase in temperature. Such drug delivery carriers are in a form of solid lipid microparticles composed of fatty acids (lauric acid or a mixture of myristic and palmitic acid), loaded with superparamagnetic iron oxide nanoparticles and anticancer drug (paclitaxel). The microparticles fulfil sever criteria including appropriate size for inhalation (1 – 5 μm), melting temperature 42 – 45°C, high drug loading efficiency, sufficient mobility in magnetic field and enhanced *in vitro* efficacy as studied in contact with healthy and cancerous lung epithelial cells in hyperthermia conditions.

Recently we are working on polymer drug delivery systems of antibiotics and quorum sensing inhibitors for the treatment of bacterial infections in patients with chronic obstructive pulmonary disease (COPD) exacerbations. The system is based on fast degrading polyanhydride microparticles /microcapsules loaded with antibiotics (gentamycin, tobramycin, azithromycin) and quorum sensing inhibitors (curcumin, linolenic acid). The microparticles /microcapsules have appropriate size for inhalation, degrade within 7 days *in vitro* and release drug cargo, which is able to kill bacteria causing COPD. The system is cytocompatible with lung epithelial cells as shown by *in vitro* tests.

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