

**Konjac glucomannan microcarriers and macrophages – a promising interaction in lung diseases treatment**

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While pulmonary drug delivery requires engineering suitable delivery systems, alveolar targeting of drugs has been studied in recent years as an approach to treat some lung diseases. This work explores the potential of konjac glucomannan (KGM) as matrix material of microcarriers targeted to alveolar macrophages, relevant actors in diseases such as tuberculosis, focusing on the analysis of particle-macrophage interaction. Mannose units composing KGM potentially improve this interaction, fostering the phagocytosis of drug-loaded particles by pathogen-infected macrophages. Spherical convoluted KGM microcarriers with geometric diameter around 3 µm were produced by spray-drying, exhibiting suitable shape and size to be internalised by macrophages. KGM microparticles-macrophage interaction was analysed by flow cytometry after 2h exposure of macrophage-like THP-1 cells to fluorescently-labelled KGM microparticles. Approximately 100% of the sampled cells were shown to phagocytose KGM particles, which was significantly higher compared with the uptake of poly(vinyl alcohol) microcarriers (62%) of similar characteristics, used as control. Furthermore, polymer-macrophage interaction (24h) was found to not induce an inflammatory response, as the release of tumour necrosis factor-α and interleukin-8 by macrophage-like THP-1 cells was significantly lower than that induced upon exposure to lipopolysaccharide. Finally, KGM microparticles at concentrations up to 1 mg/mL demonstrated absence of toxicity in macrophage-like THP-1 cells, inducing cell viability of 77-86% (MTT assay) and minimal release of LDH comparing with the positive control (Triton X-100). KGM thus appears to be a promising material for alveolar macrophage targeting, potentiating the interaction with these cells through phagocytosis without causing any harm.