Compared in vivo toxicity in mice of lung delivered biodegradable and non-biodegradable nanoparticles.

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To design nanoparticle (NP)-based drug delivery systems for pulmonary administration, biodegradable materials are considered safe, but their potential toxicity is poorly explored.

We here explore the lung toxicity in mice of biodegradable nanoparticles (NPs) and compare it to the toxicity of non-biodegradable ones. NP formulations of poly(d,l-lactide-co-glycolide) (PLGA) coated with chitosan (CS), poloxamer 188 (PF68) or poly(vinyl alcohol) (PVA), which renders 200 nm NPs of positive, negative or neutral surface charge respectively, were analyzed for their biodistribution by in vivo fluorescence imaging and their inflammatory potential after single lung nebulization in mice.

After exposure, analysis of bronchoalveolar lavage (BAL) cell population, protein secretion and cytokine release as well as lung histology were carried out.

The inflammatory response was compared to the one induced by non-biodegradable counterparts, namely, TiO$_2$ of rutile and anatase crystal form and polystyrene (PS).

PLGA NPs were mostly present in mice lungs, with little passage to other organs. An increase in neutrophil recruitment was observed in mice exposed to PS NPs 24 h after nebulization, which declined at 48 h. This result was supported by an increase in interleukin (IL)-6 and tumor necrosis factor α (TNFα) in BAL supernatant at 24 h.
TiO$_2$ anatase NPs were still present in lung cells 48 h after nebulization and induced the expression of pro-inflammatory cytokines and the recruitment of polymorphonuclear cells to BAL. In contrast, regardless of their surface charge, PLGA NPs did not induce significant changes in the inflammation markers analyzed. In conclusion, these results point out to a safe use of PLGA NPs regardless of their surface coating compared to non-biodegradable ones.