

## Mechanisms of cellular uptake and toxicity of micro and nanofibers in intestine and lung cell models

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Due to their unique properties, advanced fibrous materials are increasingly envisaged for innovative medical applications. It is also pivotal to assess the safety of such high aspect ratio materials. In this study, poly(lactic-co-glycolic acid) (PLGA) 85:15 (Sigma, 430471) and Twaron fibers (Teijin Aramid) are utilized to better understand the mechanisms whereby fibrous particles may cause toxicity in relation to their physicochemical properties, upon inhalation or oral exposure.

5 wt% PLGA is dissolved in hexafluoroisopropanol (HFIP), resulting in electrospun fibers, thus optimizing their suitability for cellular growth. In a second attempt, PEG-mRNA is added to the PLGA solution to explore potential applications as a drug delivery system. The assessment of mRNA loaded into the fibers remains difficult since both the PLGA and mRNA absorb light at 260 nm, while the acidic solvent quenches the signal of intercalating dyes. PEG-mRNA was not also detectable by using gel electrophoresis technique.

Cutting is achieved by ultrasonication with a working frequency of 20 kHz, an amplitude of 80% with the total run time up to 8 mins.

A streamlined process is employed to transform Twaron into aramid fibers. Ball milling is made for varying durations: 40 mins, 4 h, and 8 h, resulting in short fibers measuring between 0.1 mm and 1 mm in length after a 40 min period. Another endeavor is made to cut Aramid fibers using cryotome, however this technique yields significantly lower product quantities.

As the next step, the mechanisms of cellular uptake by macrophage cells will be investigated.

The unraveling of the toxicity mechanisms triggered by fibrous particles will contribute valuable insights, guiding the development of strategies to mitigate potential health hazards.