A simple method for testing the toxicity of nanomaterials on 3D Air-Liquid Interface Human Airway Epithelia (MucilAir™)

Samuel Constant, Song Huang, Mireille CaulFuty, Rosy Bonfante, Mélanie Monachino, Rebecca Frauenfelder and Ludovic Wiszniewski
Epithelix Sàrl, 14 chemin des auxl, CH-1228 Plan-les-Ouates, Switzerland, email: epithelix@epithelix.com

We developed a simple method to deliver nanoparticles to air-liquid interface (ALI) culture systems. This patented method (PCT/IB2010/053956) uses Dextran as carrier, which allows testing a wide range of doses of nanoparticles. Briefly, the nanoparticles were diluted and mixed with the Dextran powder; small pellets were made and then applied onto the apical surface of the ALI culture. We tested the toxicity of several nanoparticles, such as ZnO, on an in vitro cell model of the human airway epithelium (MucilAir™). MucilAir™ closely mimic the morphology and functions of the normal human airway epithelium. Moreover, it has a unique shelf-life of one year, allowing chronic/long term toxicity testing. Using multiple endpoints, like trans-epithelial electrical resistance (TEER), cell viability assay (LDH), cilia beating frequency, morphology, cytokine release, etc, we determined the dose response curve of ZnO nanoparticles on MucilAir™. Toxicity of ZnO (9 nm) was observed at doses higher than 9 μg/cm². Interestingly, at 9 μg/cm² of ZnO, the epithelia had the potential to recover/repair after the exposure, while at 45 μg/cm² of ZnO, it was not the case.

Dextran Tablets Preparation

1- Dilute the chemical with the carrier at the targeted concentration and mix.
2- Make serial dilutions.
3- Compress the powder into a mold to obtain a large tablet.
4- Stamp out smaller tablets with a biopsy punch.
5- Apply on MucilAir™, incubate at 37 °C for 24 hours and measure end-points.

The advantages of MucilAir™

- It is composed of primary human respiratory cells.
- It mimics the morphology and functions of the native human airway epithelium.
- It has a unique shelf-life of 12 months.
- Epithelia from different pathologies are available (asthma, COPD, CF, allergic rhinitis).
- It is ready and easy to use.

Acute Toxicity Testing

Long Term Effect

Conclusions

1: Dextran Carrier Method is an easy and powerful method for delivering nanomaterials and/or insoluble material on apical surface ALI cultures.
2: In combination with MucilAir™, this methodology allows performing acute as well as long term and repeated dose toxicity or efficacy testing of solid chemicals or mixtures.
3: Standard Operating procedures are accessible.