In vitro assessment of chemical toxicity using human respiratory cell systems

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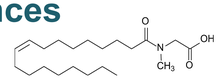
Background and purpose

There is interest in assessing the potential toxicity of surfactants due to their use in consumer products, including household cleaners, personal care items, and pharmaceuticals. Inhalation is one of the routes by which human exposure to these chemicals can happen. To evaluate the respiratory toxicity of these chemicals, a normal human bronchial epithelial cell line (BEAS-2B) and two reconstructed human respiratory epithelium (RHRE) models—a bronchial (MucilAir, Epithelix) and an alveolar (^{AX}iAECs; AlveoliX) model—were exposed to two surfactants: oleoyl sarcosine (OS) and Triton X-100 (TX).

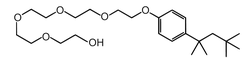
Test substances

Oleoyl sarcosine



Anionic surfactant; Negatively charged
Insoluble in water
Critical micelle concentration: 0.026 g/L (74 µM)
Acute tox (inhalation): Cat. 4 Skin irritation: Cat. 2 / Eye Irritation: Cat. 2

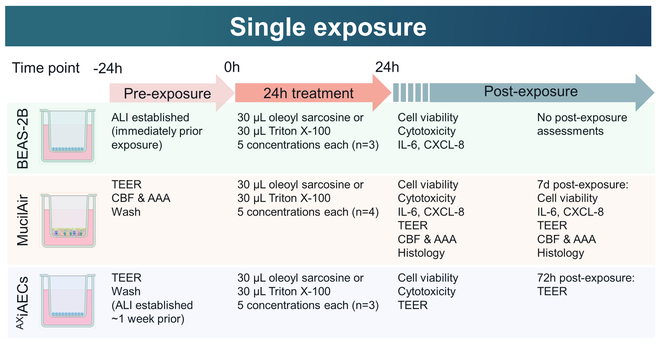
Triton X-100



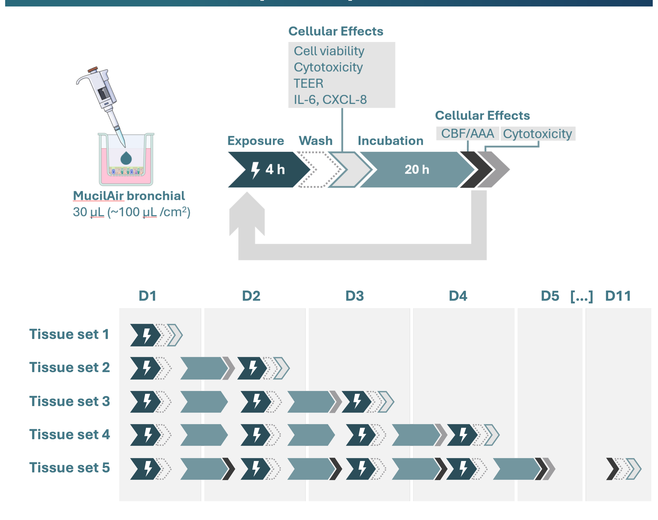
Non-ionic surfactant; Not charged
Soluble in water
Critical micelle concentration: 0.17 g/L (260 µM)
Acute tox (inhalation): No cat. Skin irritation: Cat. 2 / Eye Irritation: Cat. 1

Study design

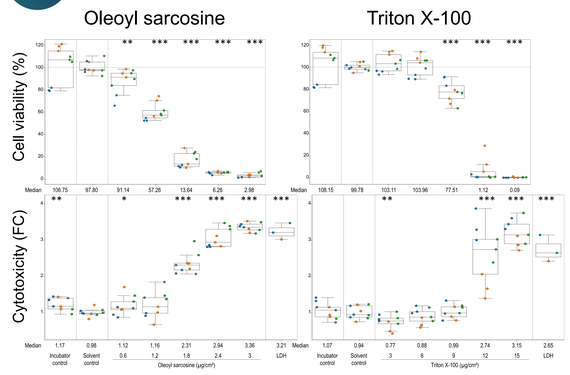
Single exposure



Repeat exposure

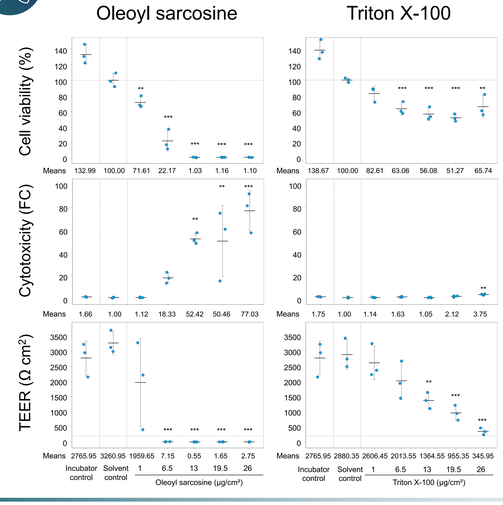


BEAS-2B – single exposure

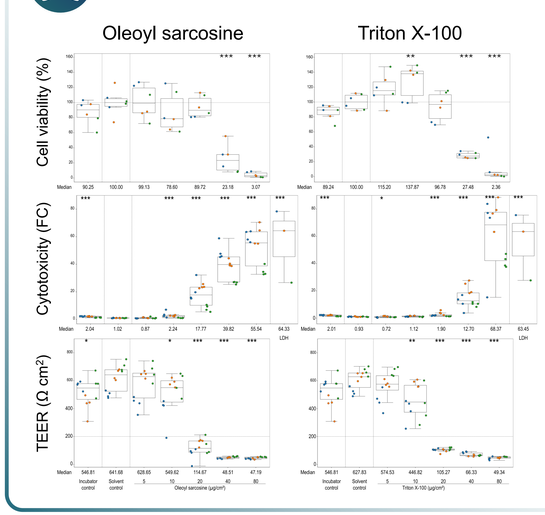


FC: fold-change relative to solvent control

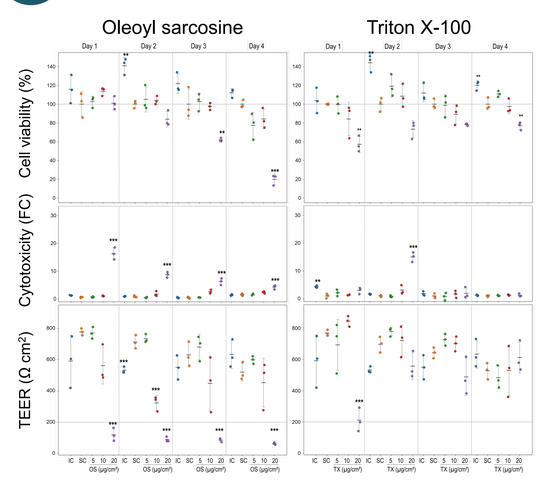
^{AX}iAEC – single exposure



MucilAir – single exposure



MucilAir – repeat exposure



Benchmark dose modelling

	Oleoyl sarcosine				Triton X-100			
	BEAS-2B	^{AX}iAEC	MucilAir		BEAS-2B	^{AX}iAEC	MucilAir	
	24h	24h	Single (24h)	Repeat (4x4h)	24h	24h	Single (24h)	Repeat (4x4h)
Cell viability	0.76	2.334	22.40	3.54	7.75	0.47	14.08	6.58
Cytotoxicity	1.40	0.69	6.77	3.72	8.60	10.642	11.96	5.68
TEER	-	0.486	7.76	5.58	-	2.895	6.28	na*

*No dose-dependent response or unexpected response in the opposite direction observed; Benchmark dose lower limit (BMDL; µg/cm²) values calculated using Benchmark dose modeling software (BMDS) Desktop (version 24.1; (https://www.epa.gov/bmds))

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Conclusions and next steps

- BEAS-2B cells and ^{AX}iAEC were generally more sensitive than MucilAir across matched endpoints, which may be attributed to the presence of a mucus layer and pseudostratified layer in MucilAir.
- Oleoyl sarcosine was generally more toxic than Triton X-100 in BEAS-2B cells and ^{AX}iAEC, but not in MucilAir.
- Single 4 h (from repeated exposure study) or 24 h exposure revealed substance-specific cellular responses, especially at higher tested concentrations.
- Acute concentration seems to drive effects more than exposure frequency for these fast-acting surfactants: repeated 4×4 h dosing in MucilAir did not systematically increase sensitivity over single 4 h or 24 h exposures, consistent with a rapid mode of action.
- These study designs and data informed an ongoing multi-laboratory study testing up to 22 chemicals in MucilAir to assess respiratory tissue irritation.
- Additional testing of ~15 surfactants is planned in MucilAir.