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Assessment of the potential health hazard of fibrous glaucophane

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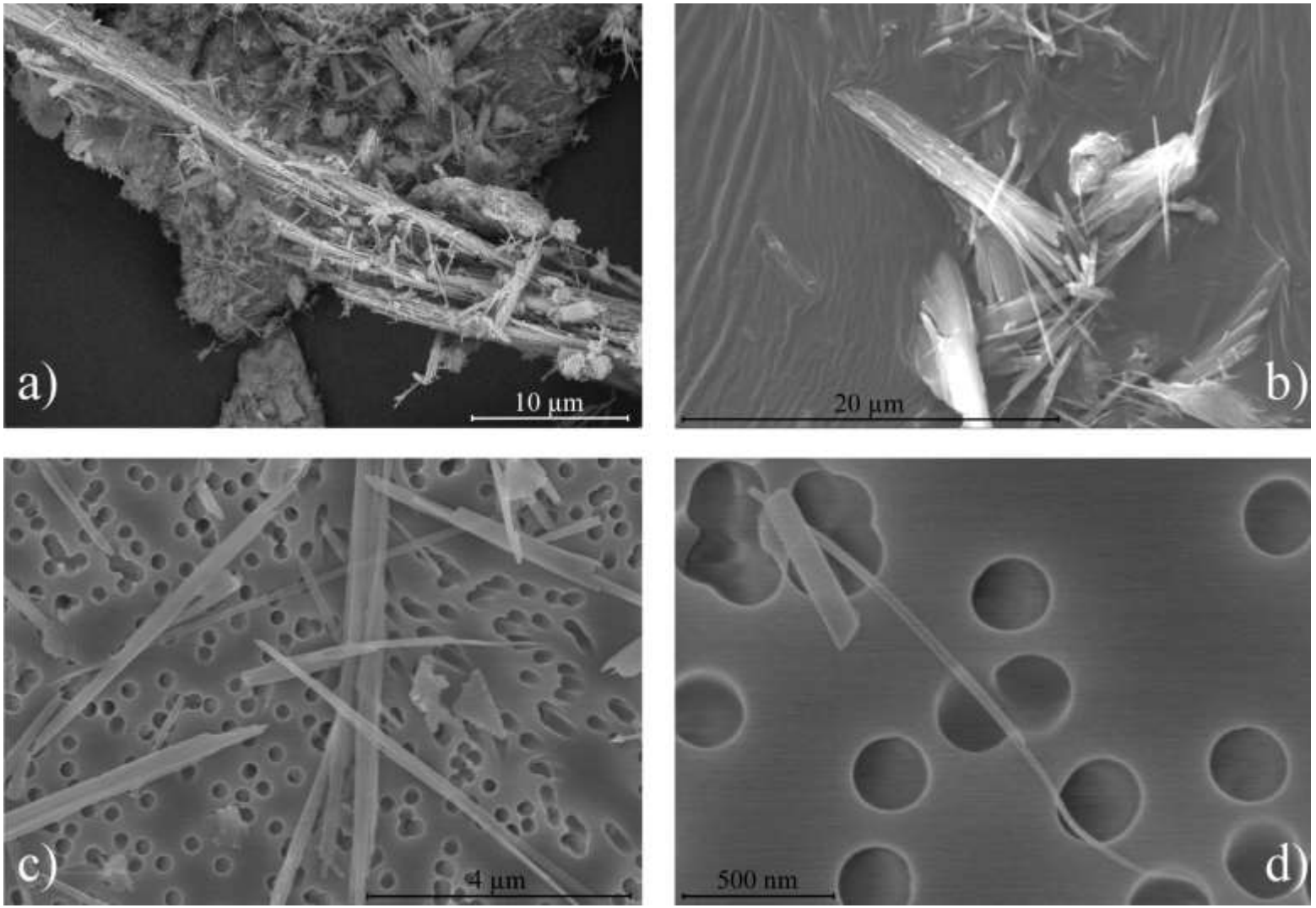
Glaucophane is a widespread sodium amphibole that can occur with a fibrous habit resembling the regulated amphibole asbestos minerals.



Representative SEM (a and b) and TEM (c and d) images of the glaucophane fibrous particles found in the blueschist sample from Franciscan Complex (California, USA).

In California (USA), the metamorphic blueschist occurrences within the Franciscan Complex are commonly composed of fibrous glaucophane. Recently, these rocks were being excavated in California for construction purposes (*e.g.,* the Calaveras Dam Replacement Project).

The potential toxicity/pathogenicity of glaucophane from the Franciscan Complex has been assessed using the fibre potential toxicity model (FPTI) model and specific in vitro toxicity tests. FPTI is an analytical tool to predict the toxicity/pathogenicity of minerals fibres, based on physical/chemical and morphological parameters that induce biochemical mechanisms responsible for *in vivo* adverse effects. This model delivers an **FPTI index** aimed at ranking the toxicity and pathogenicity of a mineral fibre.

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Characterization and assessment of the potential toxicity/pathogenicity of fibrous glaucophane

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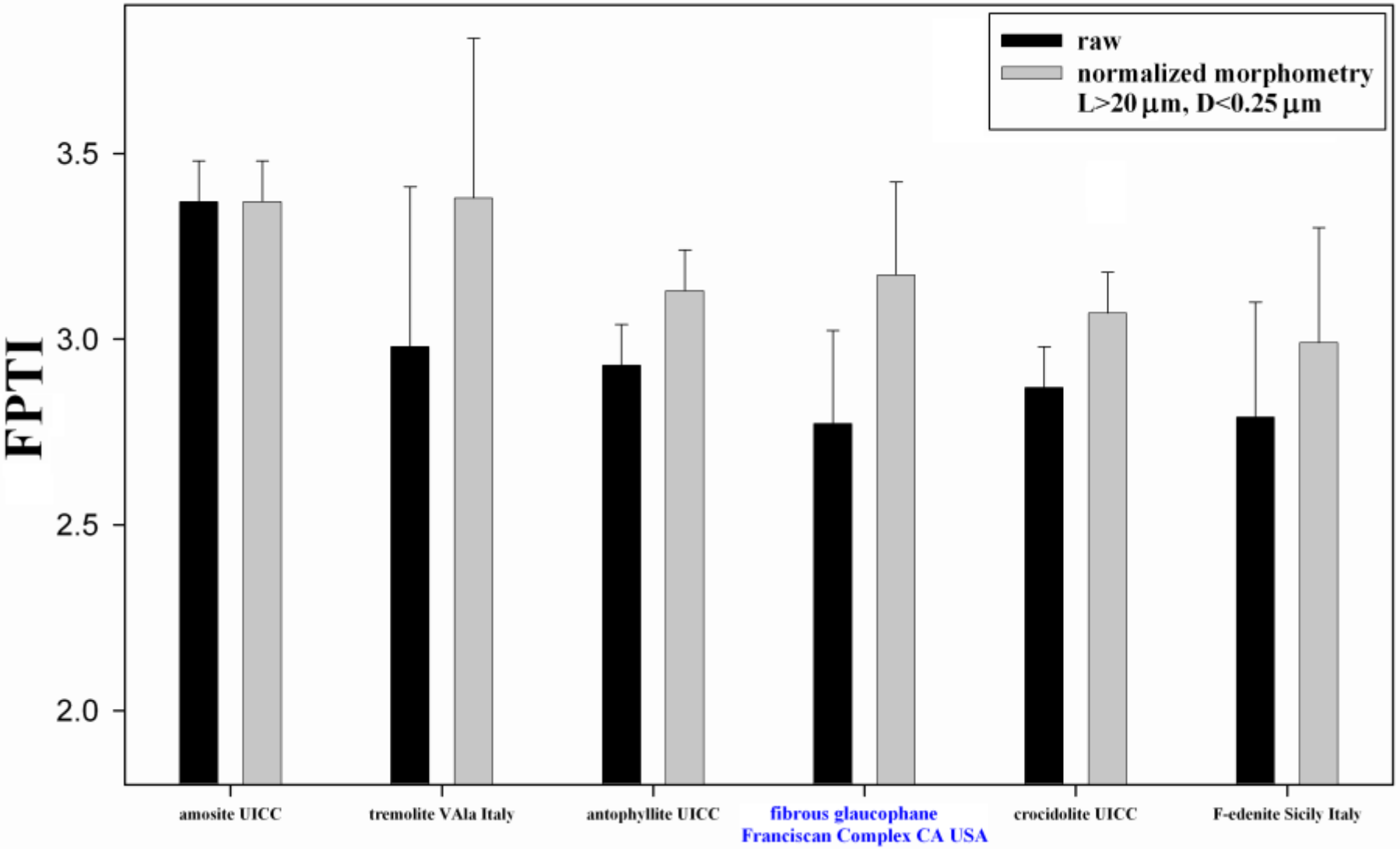
The complete description of the FPTI model and the parameters it considers is found in the following reference papers:

- Gualtieri, A.F., (2018). Towards a quantitative model to predict the toxicity/pathogenicity potential of mineral fibers. Toxicol. Appl. Pharmacol. 361, 89-98.
- Gualtieri, A.F., Mossman, B.T., Roggli, V.L., (2017). Towards a general model for predicting the toxicity and pathogenicity of minerals fibres, in: Gualtieri, A.F., (Ed.), Mineral Fibres: Crystal Chemistry, Chemical-Physical Properties, Biological Interaction and Toxicity. European Mineralogical Union-EMU Notes in Mineralogy, London, pp. 501-526.
- Mossman, B.T., Gualtieri, A.F., 2020. Lung Cancer: Mechanisms of Carcinogenesis by Asbestos, in: Anttila, S., Boffetta, P., (Eds.), Occupational Cancers. Springer, Heidelberg, pp. 239-256.

To calculate the FPTI of fibrous glaucophane and predict its toxic/ pathogenic potential, the following parameters are considered.

Parameter	Major adverse effect	Major pathobiological process
Morphometric		
length L	frustrated phagocytosis	Inflammation and oxidative stress
diameter D	frustrated phagocytosis	inflammation and oxidative stress
crystal curvature	reduced surface adhesion of proteins/cells	inflammation and oxidative stress?
crystal habit	airways deposition depth	inflammation and oxidative stress
fiber density	airways deposition depth	inflammation and oxidative stress
hydrophobic character of the surface	Interaction with biopolymers, phagocytosis	inflammation and oxidative stress?
surface area	airways deposition depth, frustrated phagocytosis	(chronic) inflammation and oxidative stress
Chemical		
Total iron content	Production of ROS	DNA damage and inflammation
ferrous iron	Production of ROS	DNA damage and inflammation
Surface ferrous iron/iron nuclearity	Production of ROS	DNA damage and inflammation
content of metals other than iron	Production of ROS	DNA damage and inflammation
Biodurability		
dissolution rate log(R)	frustrated phagocytosis	Inflammation
velocity of iron release	production of ROS	inflammation
velocity of silica dissolution	production of ROS?	oxidative stress and inflammation?
velocity of release of metals	ROS production	DNA damage, inflammation, …
Surface activity		
ξ potential	production of ROS and hemolysis	Inflammation
fibers' aggregation	frustrated phagocytosis	inflammation
Cation exchange in zeolites	interference with ER cross-talk?	apoptosis, necrosis?

FPTI of fibrous glaucophane



Potential toxicity/pathogenicity of glaucophane from the Franciscan Complex

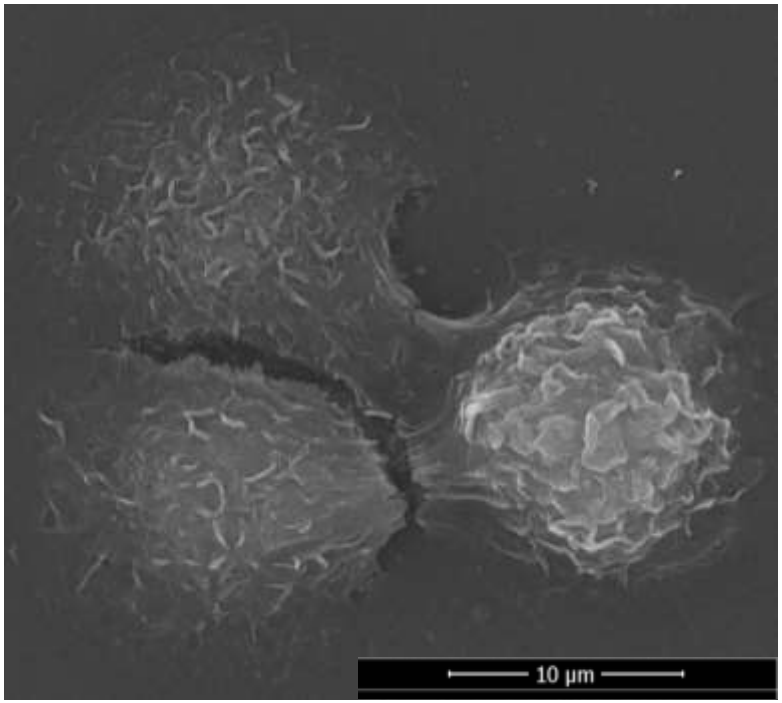
The calculated toxicity/pathogenicity potential of fibrous glaucophane is markedly greater than that of chrysotile and comparable to that of asbestos amphibole fibres supporting the application of the precautionary approach when excavation activities regard fibrous glaucophane-rich blueschist rocks.

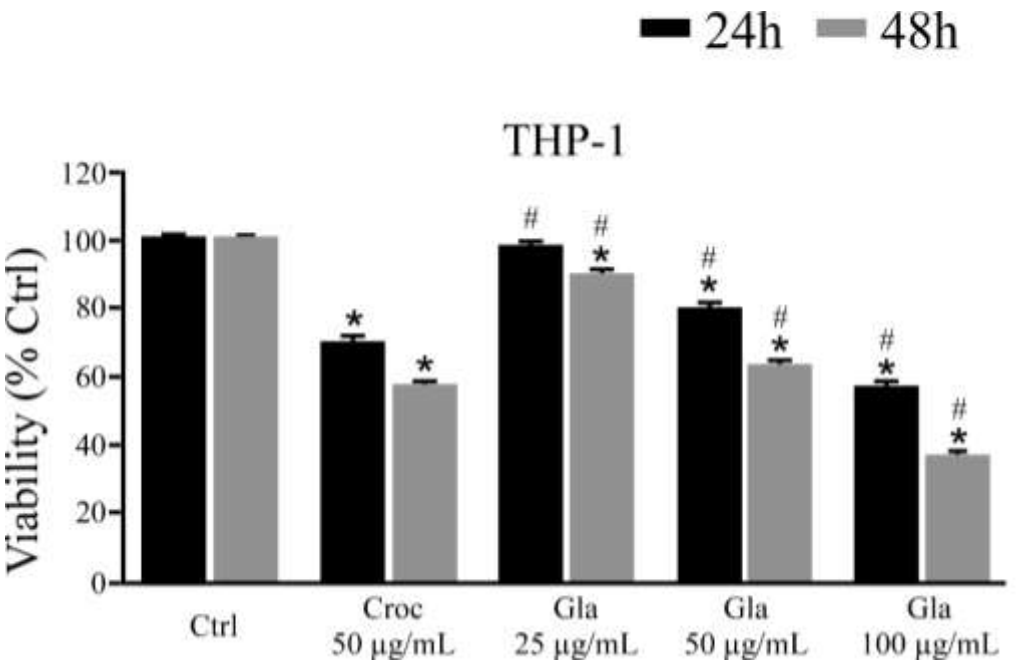
Research in progress

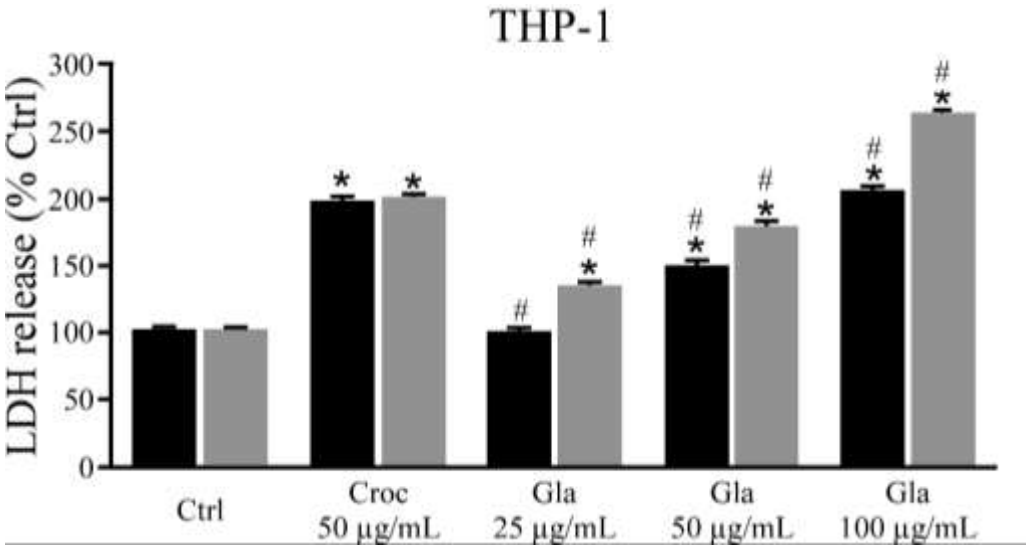
Our currently studies aim to determine whether fibrous glaucophane can induce an *in vitro* toxicity effect on lung cells. Biological responses of cultured human lung cells (THP-1 and Met-5A) following 24 and 48h of exposure to different doses of fibrous glaucophane (25, 50 and 100 µg/mL), are determined by Alamar Blue viability, Extra-cellular lactate dehydrogenase (LDH). Crocidolite UICC asbestos (100 µg/mL) is also tested for comparison.

Preliminary results

THP-1 cells

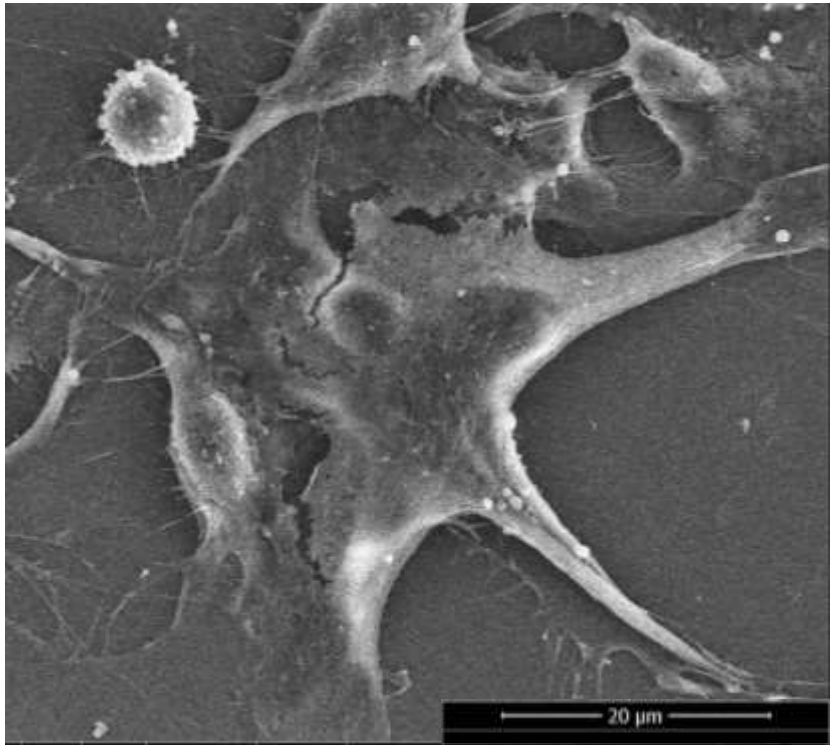


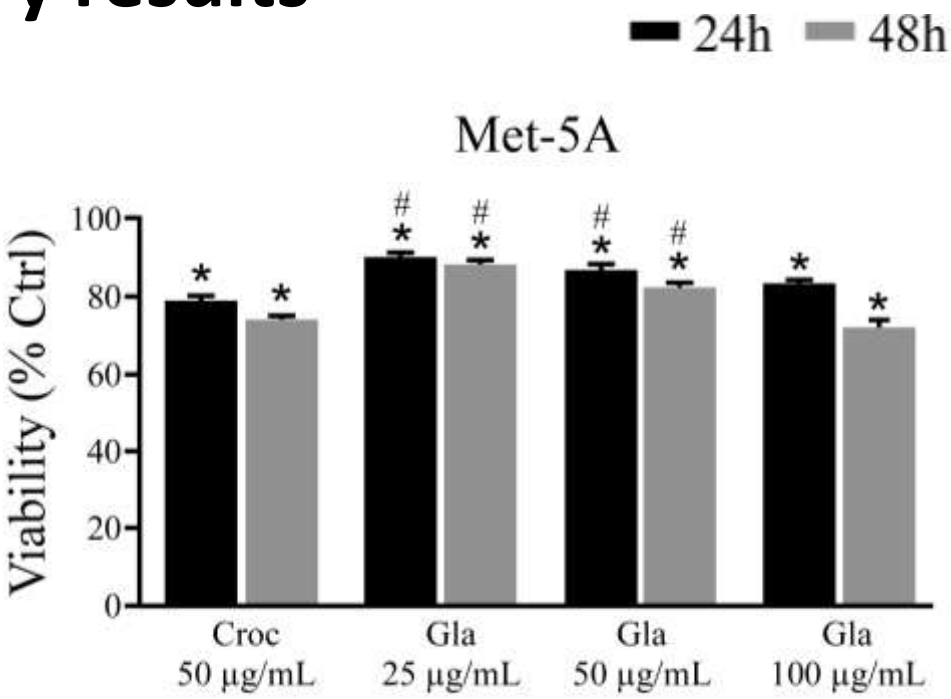


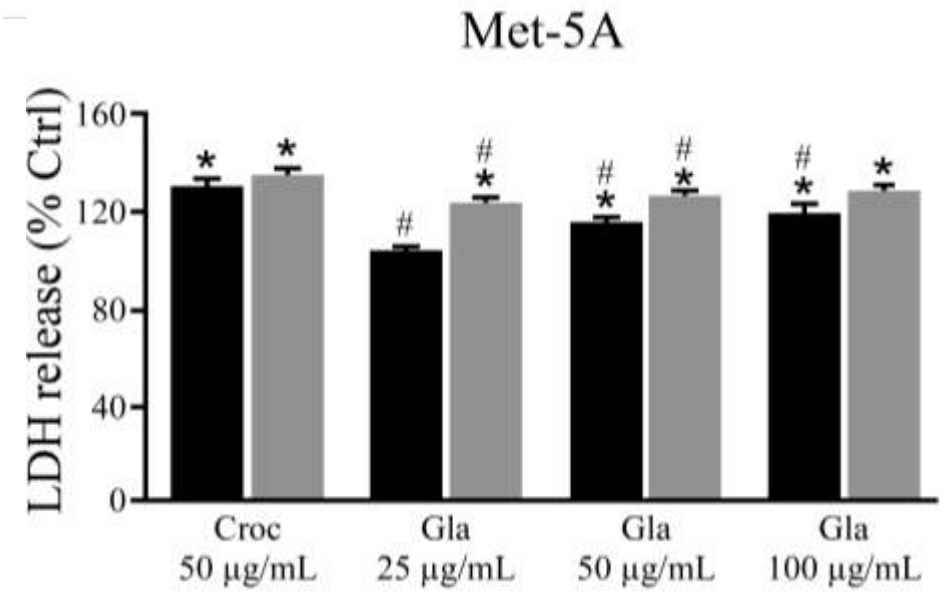


Preliminary results

Met-5A cells







Preliminary results

Preliminary results of the *in vitro* tests showed that fibrous glaucophane (Gla) may induce a decrease in cell viability and an increase in LDH release in tested cell cultures in a concentration dependent mode. Overall, the rank of the investigated fibres in increasing order of cytotoxicity is: Gla (25 µg/mL) < Gla (50 µg/mL) < crocidolite (50 µg/mL) < Gla (100 µg/mL). For both the cells lines (THP-1 and Met-5A), Gla was able to induce DNA damage. Moreover, it was found that Gla can induce the formation of ROS. The chemical-structural features and biological reactivity of Gla confirm that this mineral fibre is a toxic agent. Although Gla induced lower toxic effects compared to the carcinogenic crocidolite, the inhalation of its fibres may be hypothetically responsible for the development of lung diseases.