PRIN: PROGETTI DI RICERCA DI RILEVANTE INTERESSE NAZIONALE

Bando 2017 - Prot. 20173X8WA4

FIBRES: a multidisciplinary mineralogical, crystal-chemical and biological project to amend the paradigm of toxicity and cancerogenicity of mineral fibres

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Workshop 6-7 luglio 2023

Unità di Urbino

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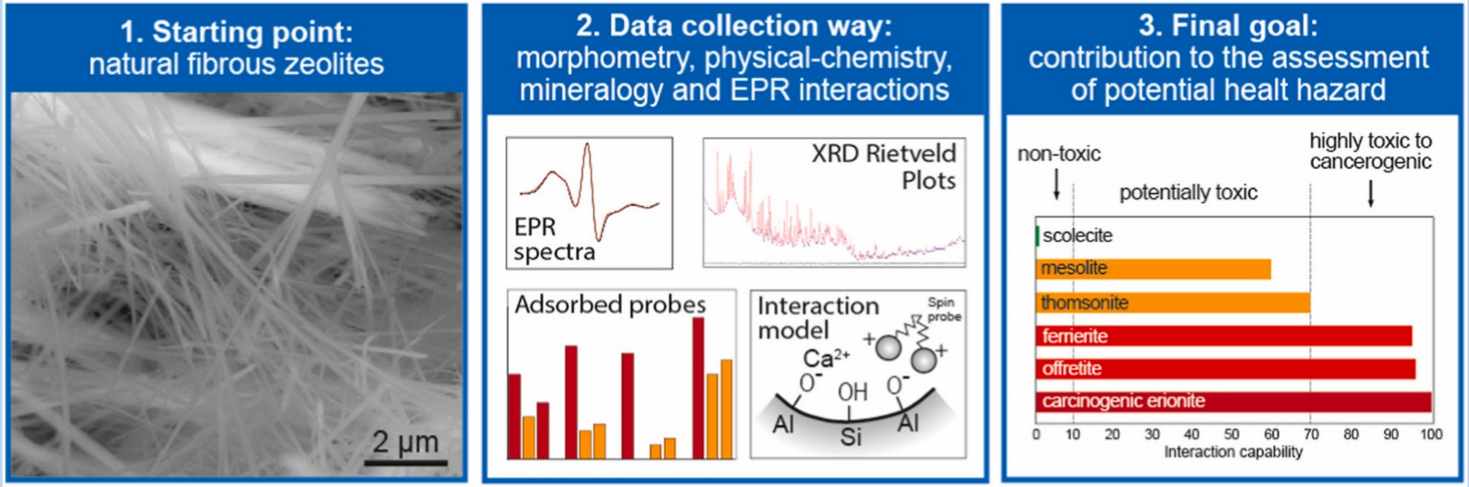
The Research Unit of Urbino has focused its activity on two main subjects:

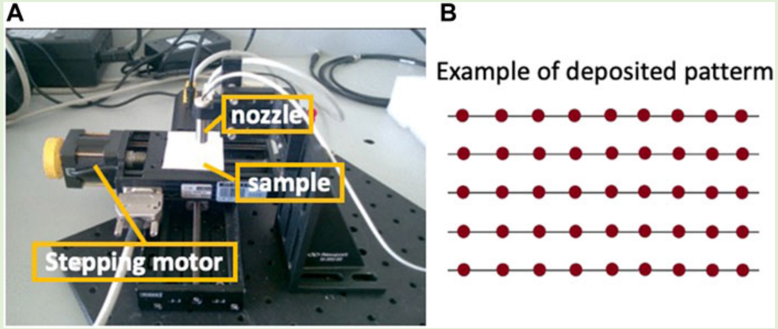
1. Investigation of morphological, mineralogical, and physico-chemical features of potentially toxic natural fibrous zeolites and other possibly hazardous mineral fibres*



*Some aspects of this topic benefited from the contribution of the Rome and Modena research units

2. Design of a novel method to prepare fibres depositions to be used for toxicological experiments

(Giancarlo Della Ventura)



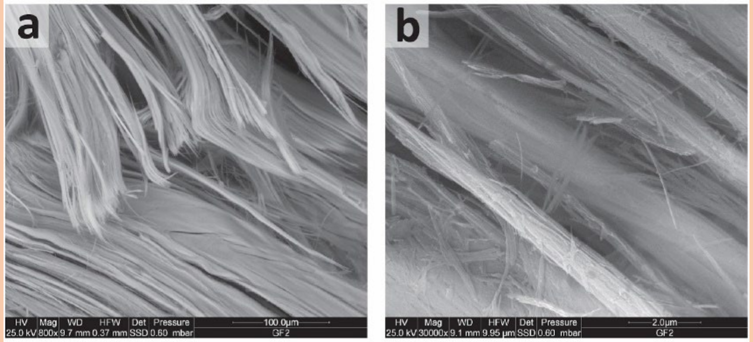
As regard the first subject, Giordani et al. (2022a) investigated three samples of natural zeolites: an extremely fibrous erionite (**GF2**), a highly fibrous mesolite (**GF3a**) and a prismatic thomsonite (**GF3b**).

GF2 erionite

fibrils in the range of inhalable and most carcinogenic fibres

highest Si/Al ratio (3.38)

highest values of BET-specific surface area (8.14 m^2/g).

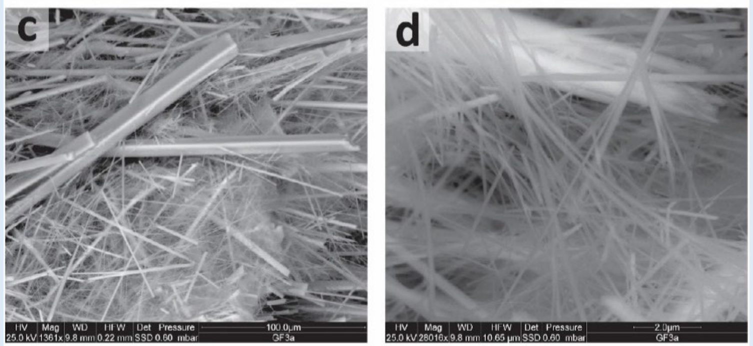


GF3a mesolite

tiny fibres and fibrils in the range of carcinogenic fibres

lower Si/Al ratio (1.56)

smaller values of BET-specific surface (1.55 m^2/ g)

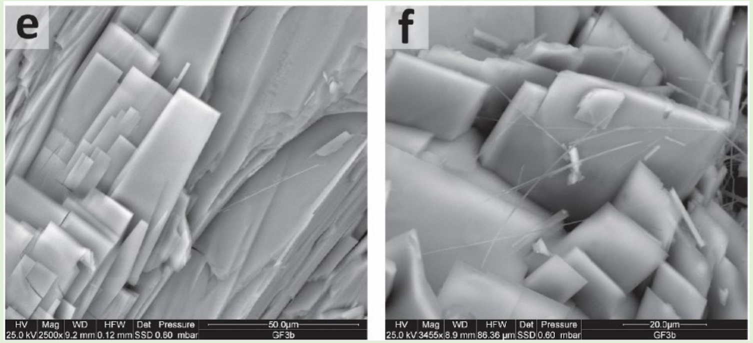


GF3b thomsonite

massive crystals with very few thin fibres

lowest Si/Al ratio (1.23)

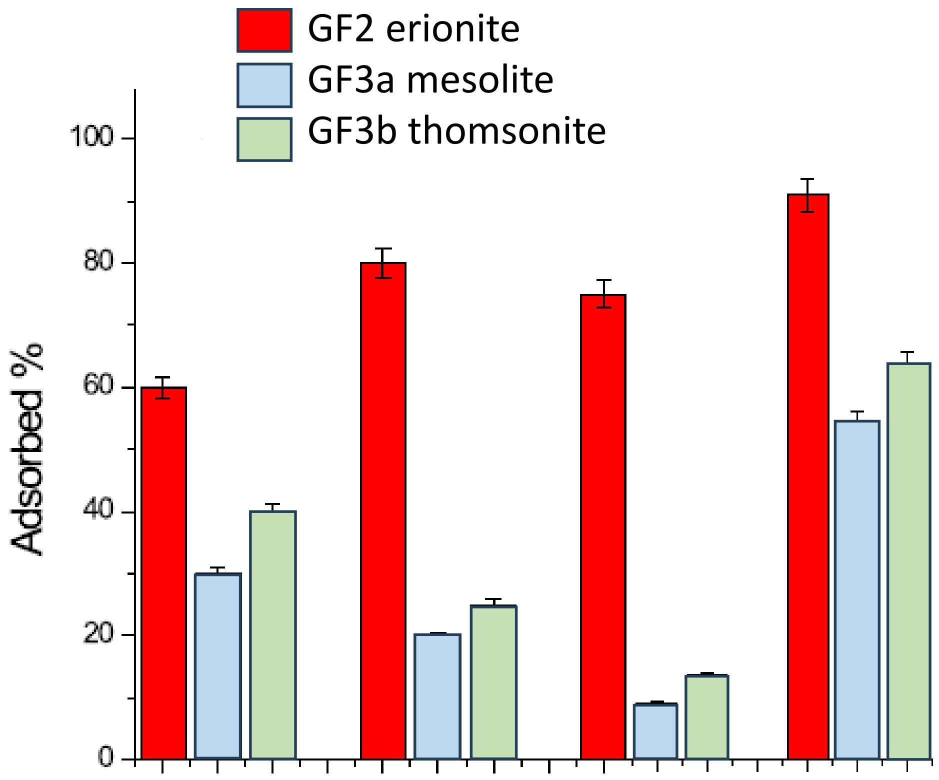
lowest BET-specific surface area (0.38 m^2/g).



Giordani M., Mattioli M., Cangiotti M., Fattori A., Ottaviani M.F., Betti M., Ballirano P., Pacella A., Di Giuseppe D., Scognamiglio V., Hanuskova M., Gualtieri A.F. (2022a). *Characterisation of potentially toxic natural fibrous zeolites by means of electron paramagnetic resonance spectroscopy and morphological-mineralogical studies*. CHEMOSPHERE, 291, 133067-133082, doi: 10.1016/j.chemosphere.2021.133067

These data become much more helpful when integrated and compared with analysing selected spin probes' electronic paramagnetic resonance (EPR) spectra.

EPR data reveal that GF2 has a homogeneous site distribution intercalating more and less hydrophilic sites. Consequently, the GF2 surface interacts well with all spin probes, representing the chemical moieties in biological environments.

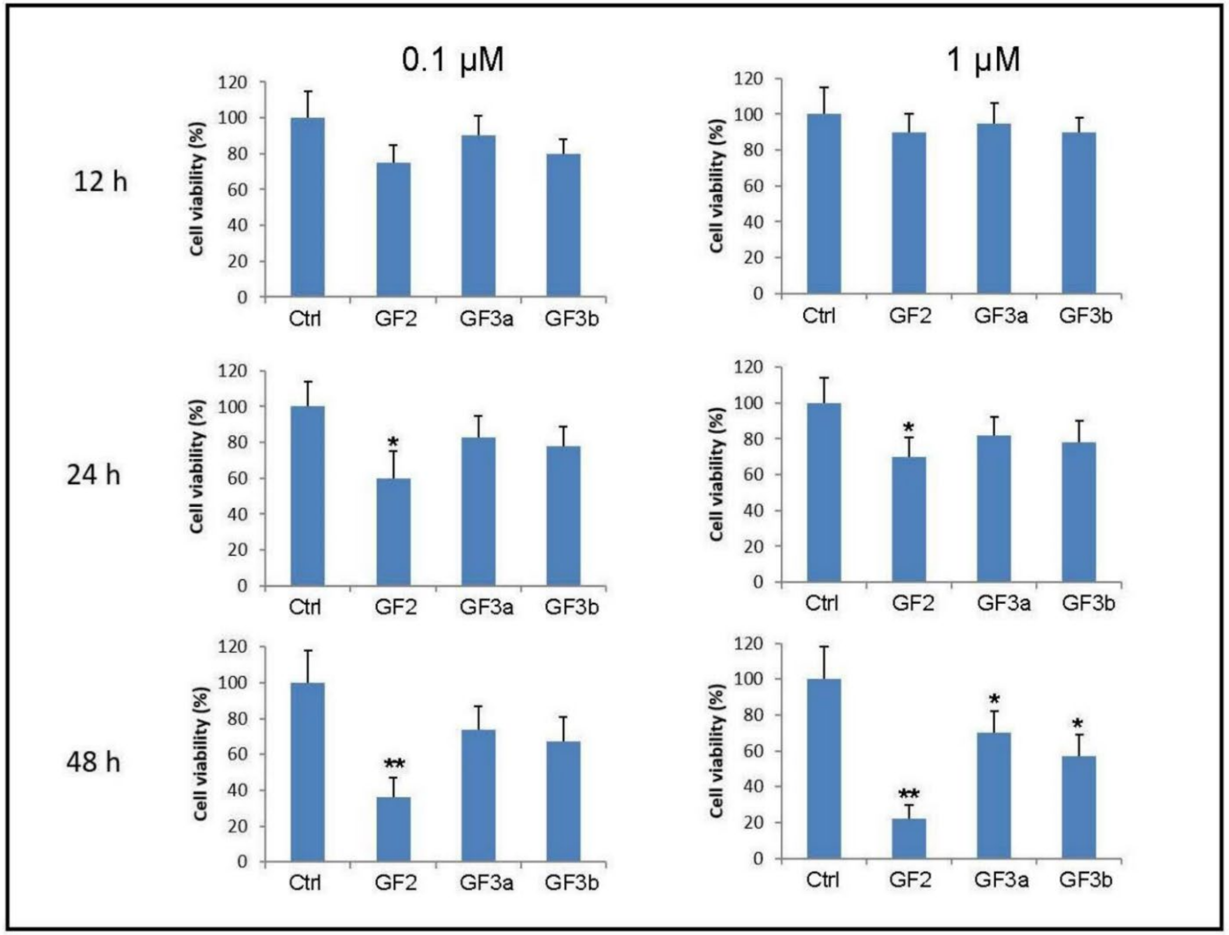


These results suggest that **the potential toxicity of a fibrous mineral is most likely related to the interacting capability of the fibres and their interaction sites**. This interaction capability increases by increasing the surface area, the availability of the interaction sites, and different well-distributed polar sites. Therefore, we expect **potential toxicity to decrease in the series order erionite ≫ mesolite > thomsonite.**

These indications were also tested by an *in vitro* study (Betti et al., 2022), to determine if and how these fibrous zeolites induce toxic effects on two different in vitro cellular models, the adherent murine hippocampal (HT22) and human immortalized T lymphocyte (Jurkat) cell lines.

Results showed a cytotoxic effect of erionite in both cellular models and revealed different toxic behaviour of the mesolite and thomsonite fibres, suggesting other potential mechanisms of action.

The outcome of this study would be a first step for further research on fine biochemical interactions of zeolite fibres with cells and future in vivo investigations.

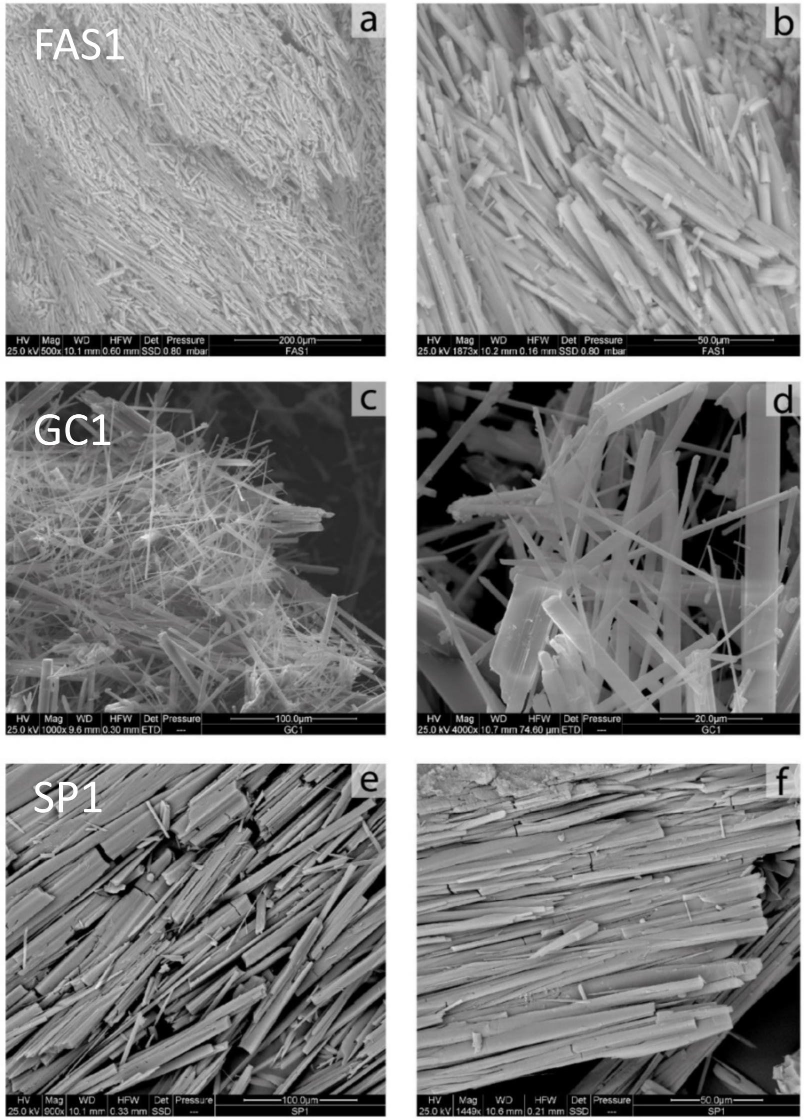


Evaluation of potential toxicity of GF2, GF3a, GF3b fibrous zeolites in Jurkat cell line. The histograms show cell viability after 12, 24, and 48 h of GF2, GF3a, and GF3b exposure at the concentration of 0.1 µM and 1 µM. Each value is expressed as a percentage ± SD (N = 3 independent experiments performed in triplicate; * $p < 0.05$, ** $p < 0.01$ vs. Ctrl).

Betti M., Nasoni M.G., Luchetti F., Giordani M., Mattioli M. (2022). *Potential Toxicity of Natural Fibrous Zeolites: In Vitro Study Using Jurkat and HT22 Cell Lines.* MINERALS, vol. 12, p. 988-999, doi: 10.3390/min12080988

Another contribution to the first subject come from Giordani et al. (2022b), where **three mordenite samples** from Northern Italy were investigated. Despite the size differences, all the studied mordenite samples are characterized by “respirable” fibres that could reach the lungs’ deeper parts.

WIDTH	FAS1	GC1	SP1
<3 μm	95.56%	92.02%	78%
3–5 μm	3.33%	6.27%	6.50%
>5 μm	1.11%	1.71%	15.50%
min	0.1 μm	0.1 μm	0.1 μm
max	6 μm	7 μm	8 μm
σ	1.04	1.25	2.13
LENGTH			
<20 μm	56.67%	63.82%	46%
20–100 μm	43.33%	36.18%	40.50%
100–200 μm	0	0	13.50%
min	4 μm	5 μm	4 μm
max	80 μm	70 μm	170 μm
σ	14.49	14.50	44.29
Dae (μm)	**2.69**	**1.19**	**3.91**



Giordani M., Ballirano P., Pacella A., Meli M.A., Roselli C., Di Lorenzo F., Fagiolino I., Mattioli M. (2022b). *Another Potentially Hazardous Zeolite from Northern Italy: Fibrous Mordenite*. MINERALS, vol. 12, p. 627-643, doi: 10.3390/min12050627

All the analysed samples show similar chemical characteristics: they are Na-rich (Na > Ca > K), and the Al content decrease reflects from FAS1 to GC1.

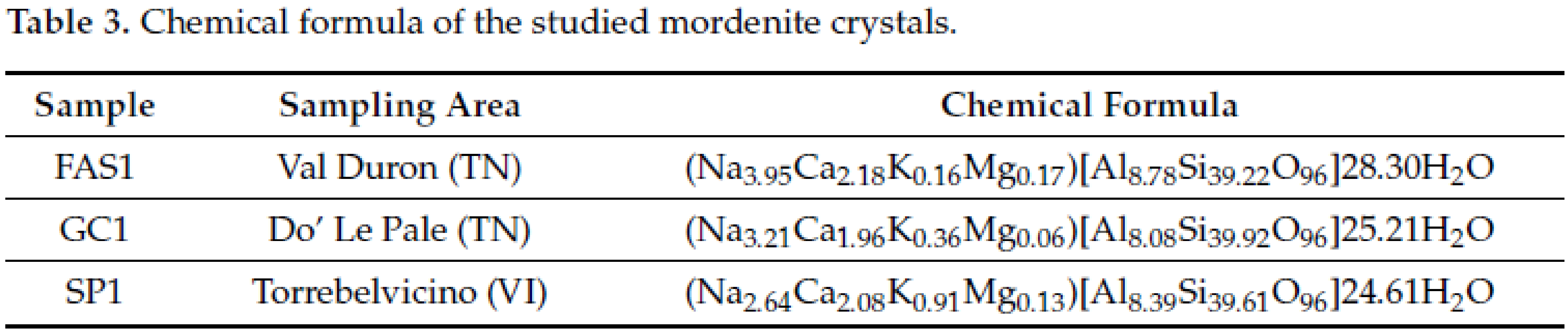


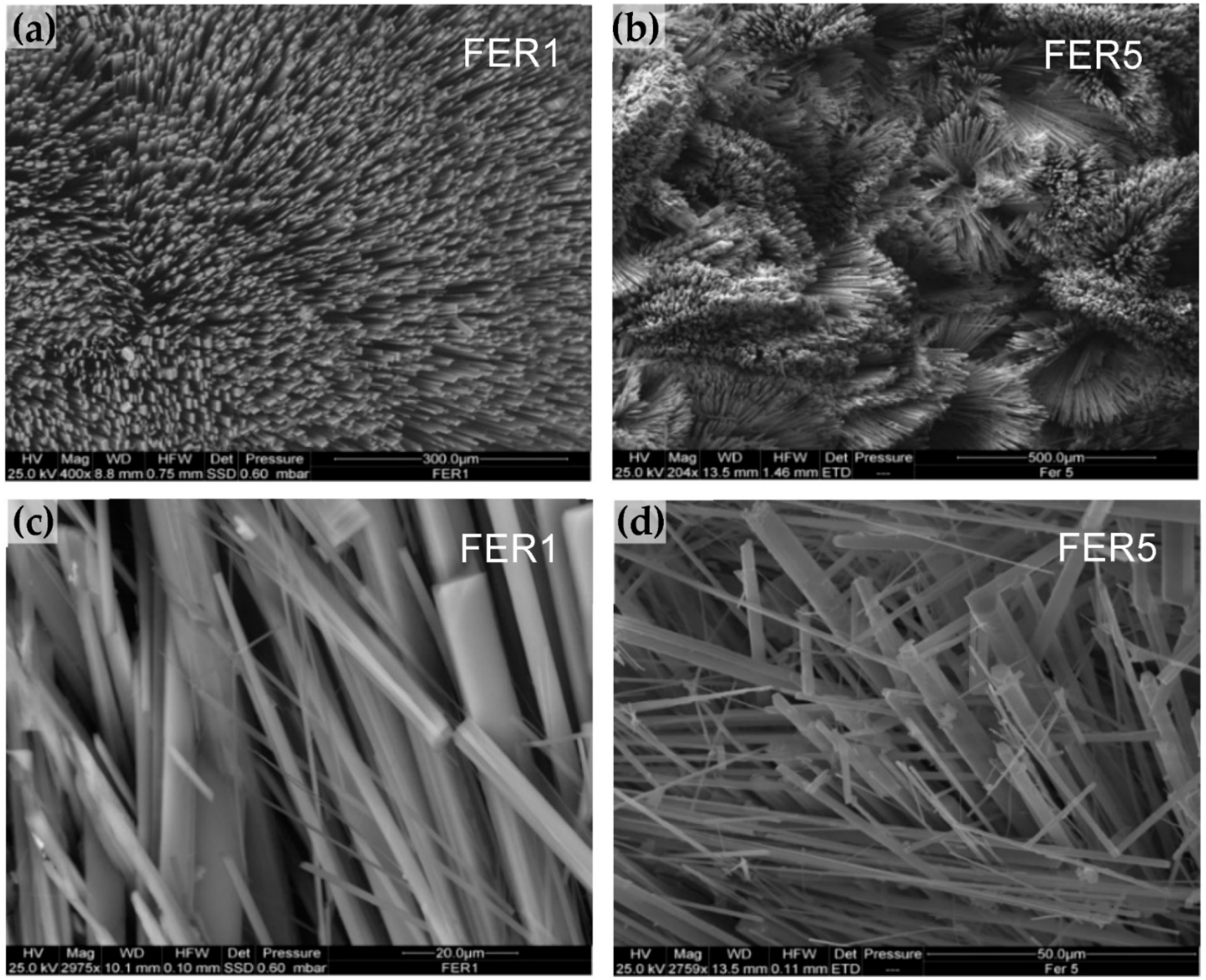
Table 3. Chemical formula of the studied mordenite crystals.

Sample	Sampling Area	Chemical Formula
FAS1	Val Duron (TN)	$(Na_{3.95}Ca_{2.18}K_{0.16}Mg_{0.17})[Al_{8.78}Si_{39.22}O_{96}]28.30H_2O$
GC1	Do' Le Pale (TN)	$(Na_{3.21}Ca_{1.96}K_{0.36}Mg_{0.06})[Al_{8.08}Si_{39.92}O_{96}]25.21H_2O$
SP1	Torrebelvicino (VI)	$(Na_{2.64}Ca_{2.08}K_{0.91}Mg_{0.13})[Al_{8.39}Si_{39.61}O_{96}]24.61H_2O$

The structural features of the investigated samples are also similar, and the unit cell volume follows the series FAS1 > SP1 > GC1, reflecting Al content decreasing. The higher Si/Al ratio of mordenite (about 4.7) compared to erionite (about 3.5) could also play an important part in its biodurability. **These results indicate that fibrous mordenite may represent a potential health hazard and should be tested for toxicity and carcinogenicity, as it could be a non-safe zeolite.**

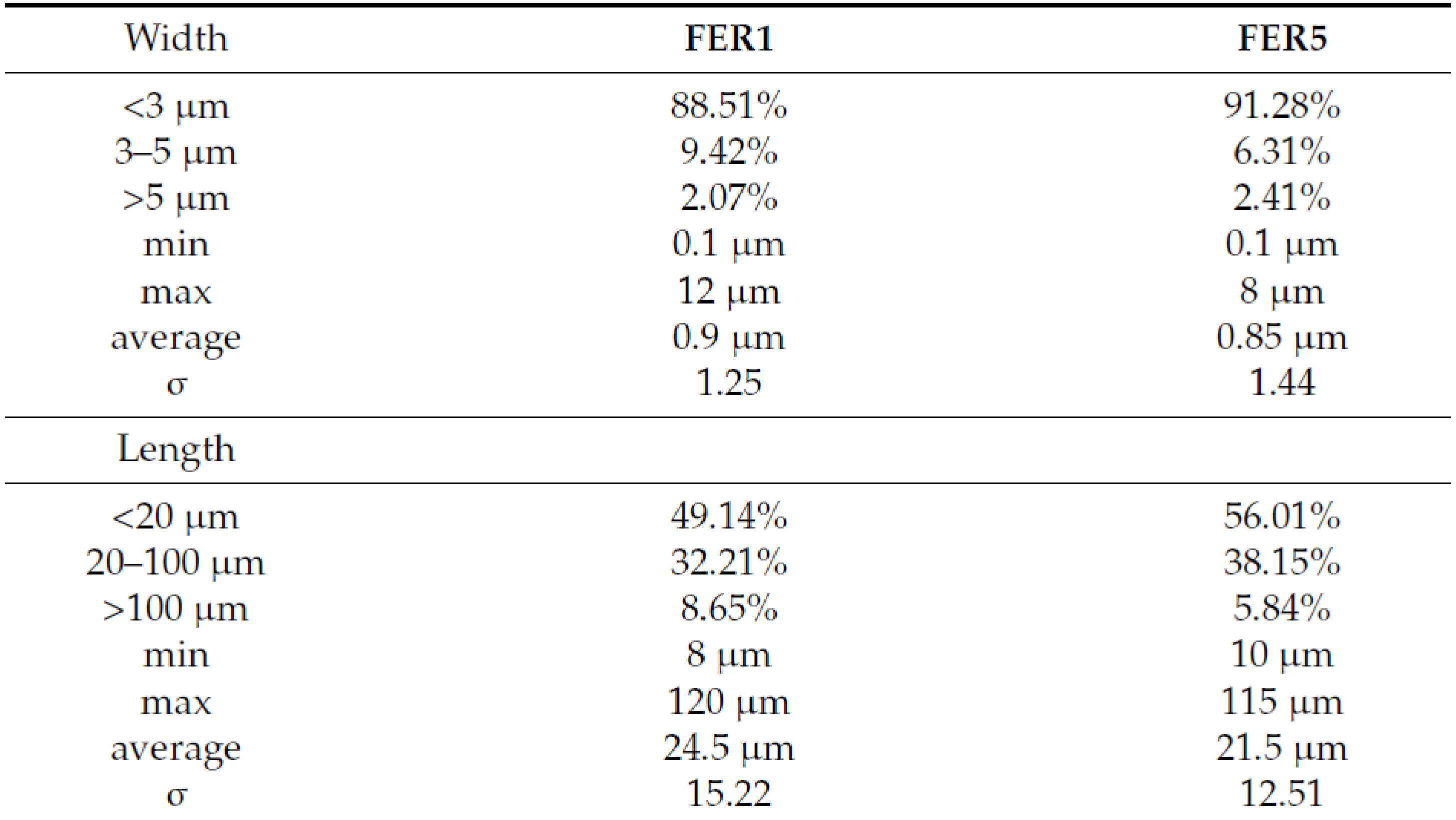
Another study (Mattioli et al., 2022) investigated the morphology, crystal structure, chemistry, and surface activity of natural **ferrierite recently found in Northern Italy**, which shows a particularly fibrous habit and chemical-physical properties very similar to the ferrierite described by Gualtieri et al. (2018).

Gualtieri et al. (2018). Is fibrous ferrierite a potential health hazard? Characterization and comparison with fibrous erionite. AMERICAN MINERALOGIST, vol. 103, p. 1044-1055, doi: 10.2138/am-2018-6508

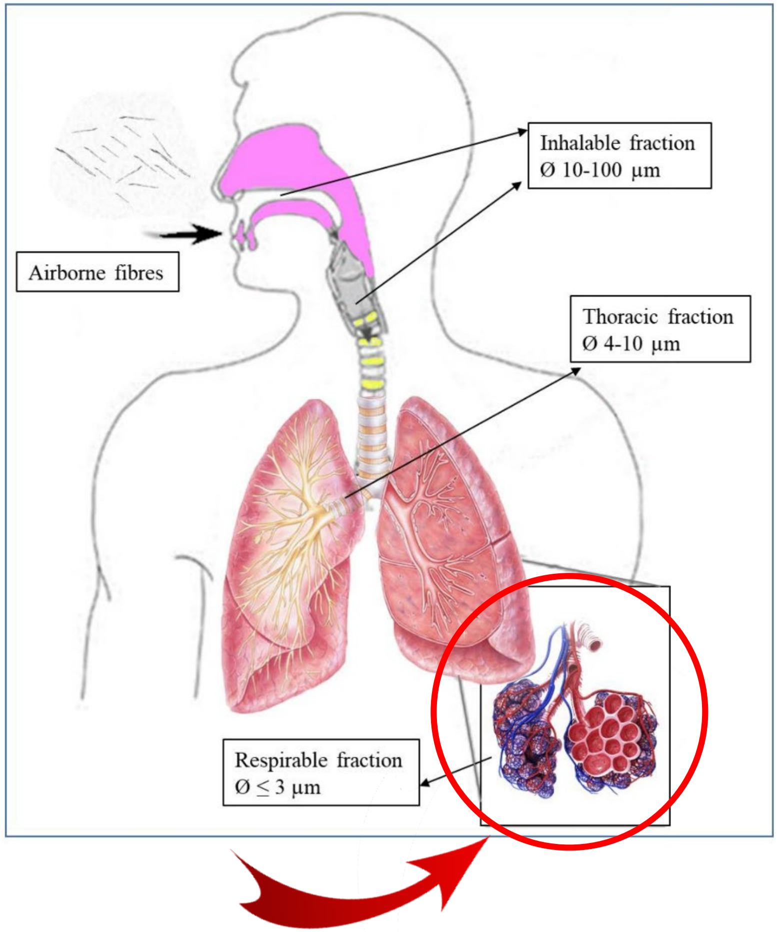


Mattioli M., Ballirano P., Pacella A., Cangiotti M., Di Lorenzo F., Valentini L., Meli M.A., Roselli C., Fagiolino I., Giordani M. (2022). *Fibrous Ferrierite from Northern Italy: Mineralogical Characterization, Surface Properties, and Assessment of Potential Toxicity*. MINERALS, vol. 12, p. 626-649, doi: 10.3390/min12050626

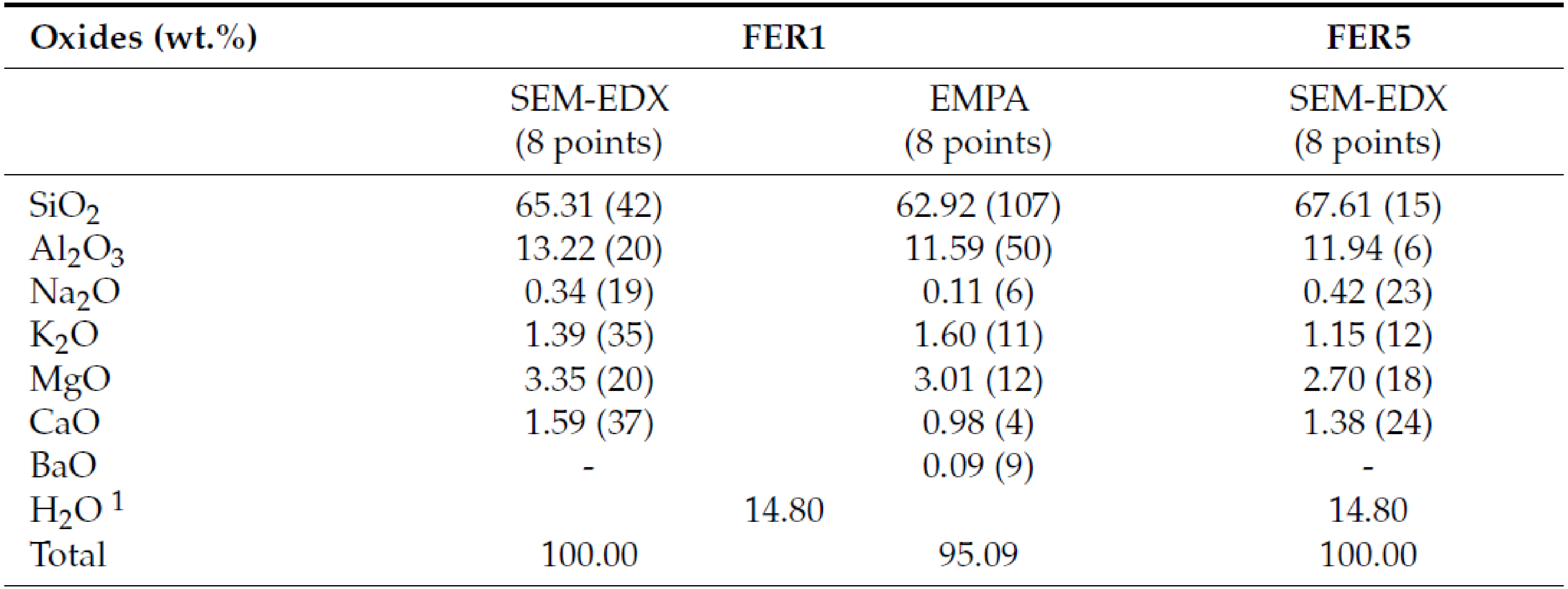
Our results show that a notable amount of ferrierite fibres are breathable (average length ~22 µm, average diameter 0.9 µm, diameter-length ratio >> 1:3) and able to reach the alveolar space (**average Dae value 2.5 µm**).



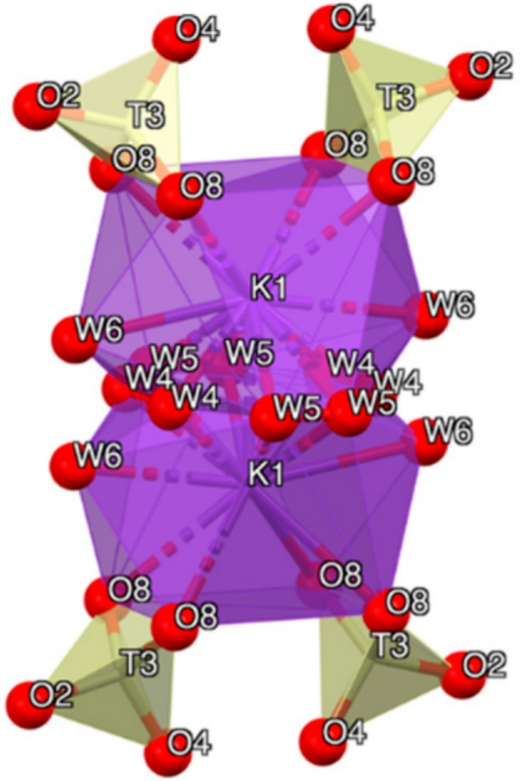
Width	FER1	FER5
<3 µm	88.51%	91.28%
3–5 µm	9.42%	6.31%
>5 µm	2.07%	2.41%
min	0.1 µm	0.1 µm
max	12 µm	8 µm
average	0.9 µm	0.85 µm
σ	1.25	1.44
Length		
<20 µm	49.14%	56.01%
20–100 µm	32.21%	38.15%
>100 µm	8.65%	5.84%
min	8 µm	10 µm
max	120 µm	115 µm
average	24.5 µm	21.5 µm
σ	15.22	12.51
Dae (µm)	**2.59**	**2.42**



The prevailing extra-framework cations are in the Mg > (Ca ≈ K) relationship, R is from 0.81 to 0.83, and the Si/Al ratio is high (4.2-4.8). The <T-O> bond distances suggest the occurrence of some degree of Si,Al ordering, with Al showing a site-specific occupation preference T1 > T2 > T3 > T4.



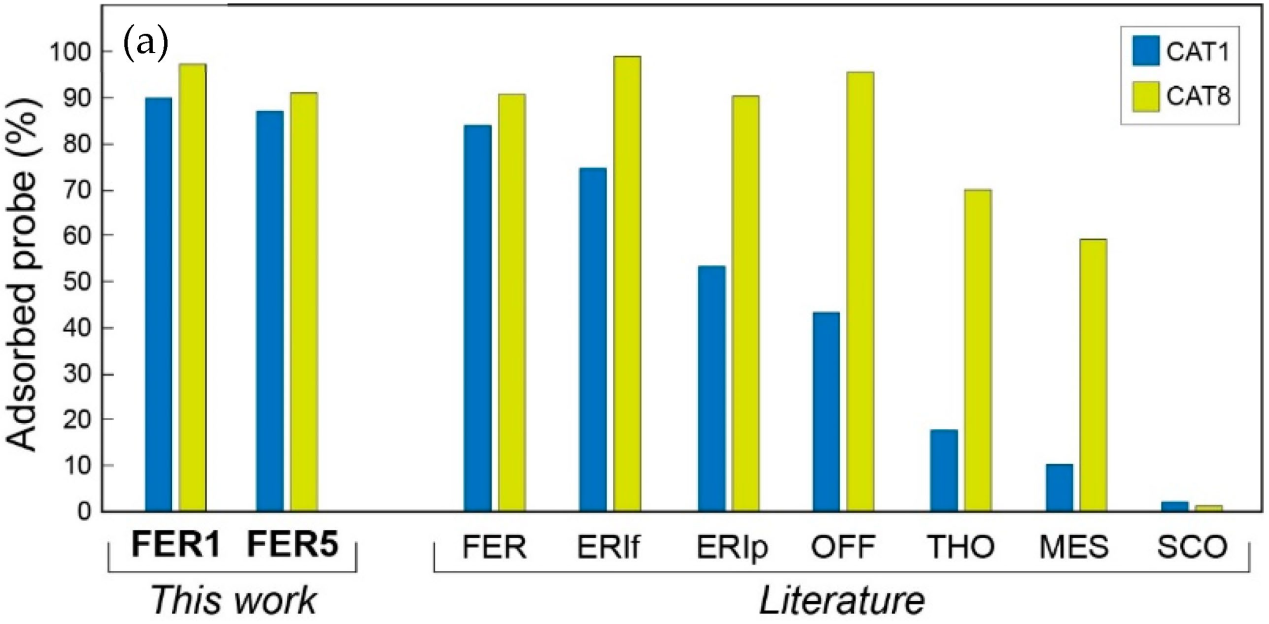
Oxides (wt.%)	FER1		FER5
	SEM-EDX (8 points)	EMPA (8 points)	SEM-EDX (8 points)
SiO_2	65.31 (42)	62.92 (107)	67.61 (15)
Al_2O_3	13.22 (20)	11.59 (50)	11.94 (6)
Na_2O	0.34 (19)	0.11 (6)	0.42 (23)
K_2O	1.39 (35)	1.60 (11)	1.15 (12)
MgO	3.35 (20)	3.01 (12)	2.70 (18)
CaO	1.59 (37)	0.98 (4)	1.38 (24)
BaO	-	0.09 (9)	-
H_2O [1]	14.80		14.80
Total	100.00	95.09	100.00



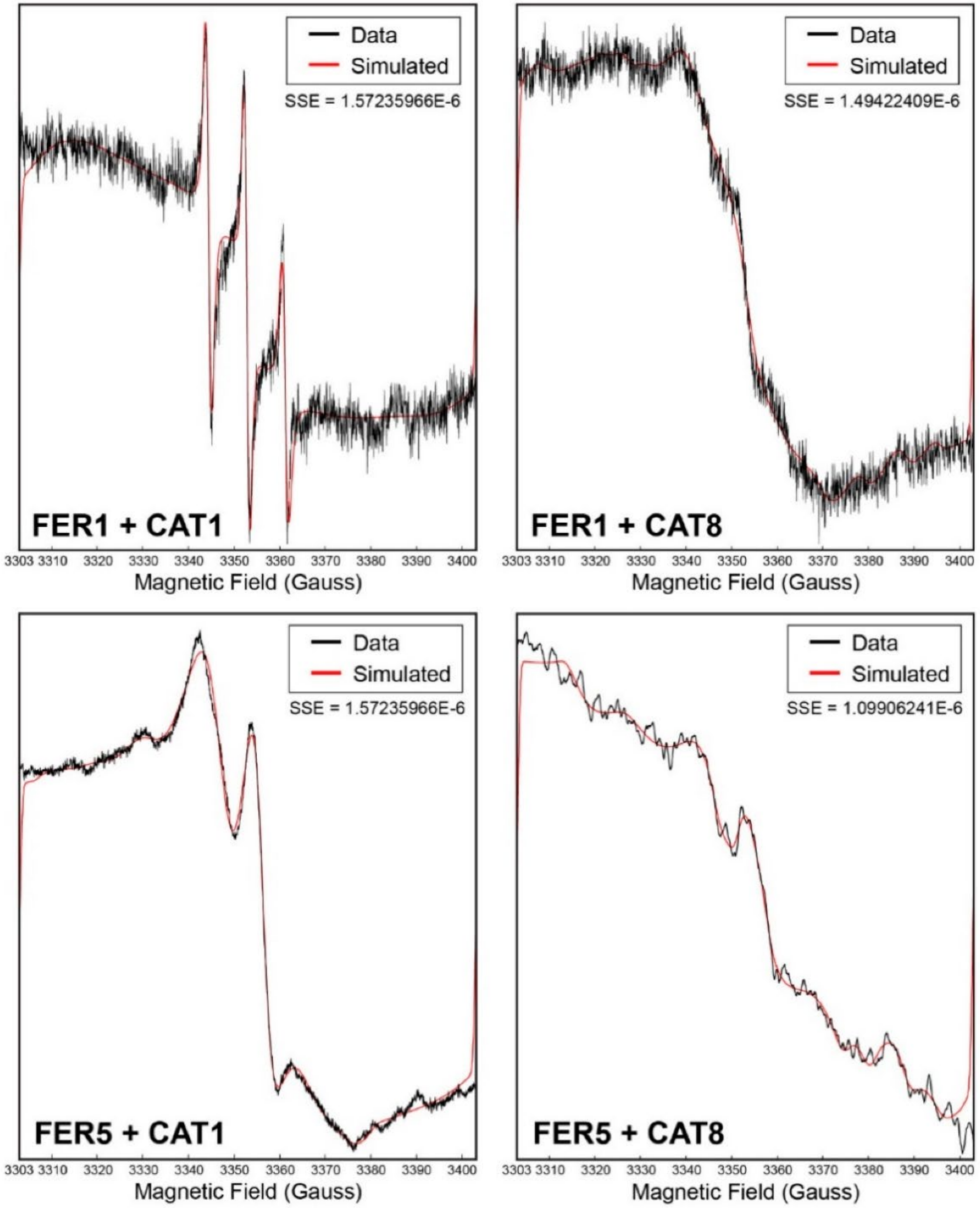
FER1 $(Mg_{2.22}K_{0.79}Ca_{0.76}Na_{0.30})[Si_{29.07}Al_{6.93}O_{72}]21.97H_2O$

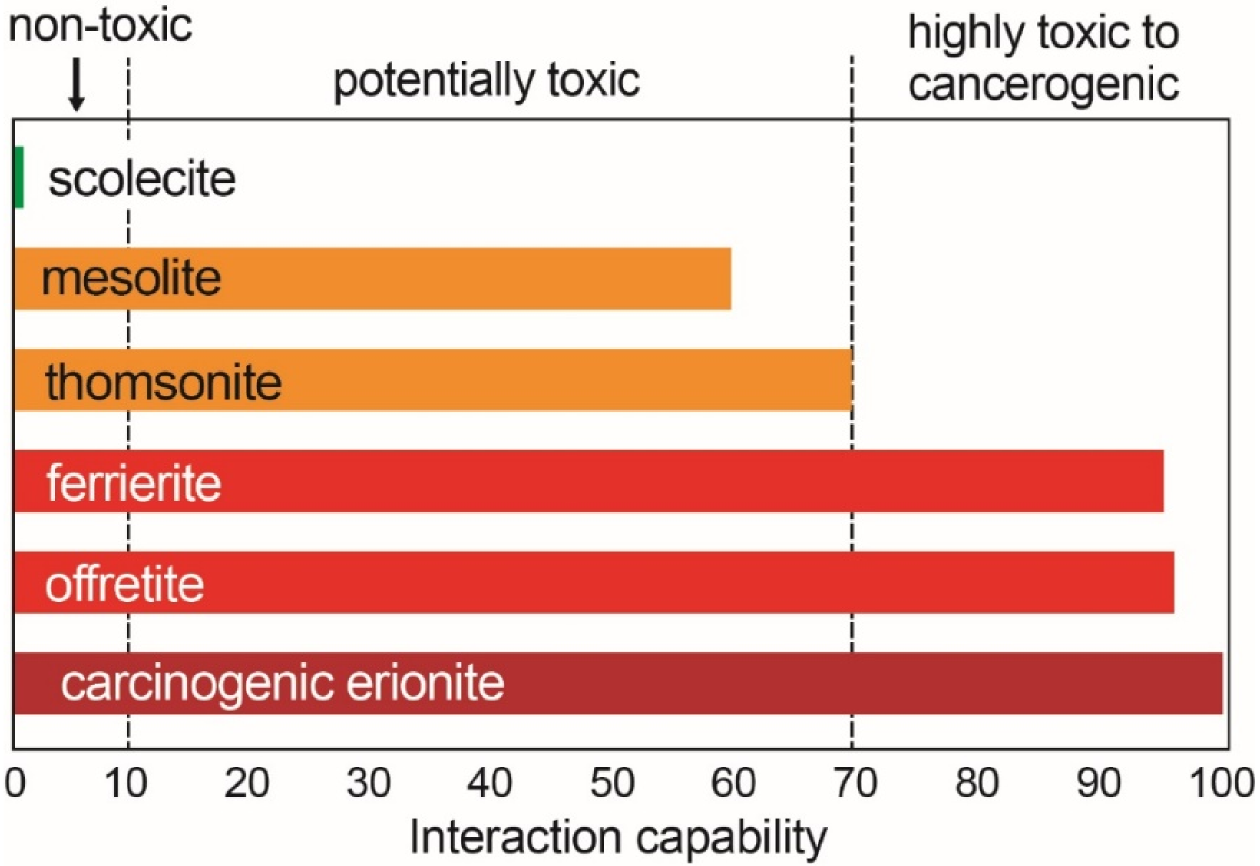
FER2 $(Mg_{1.77}K_{0.65}Ca_{0.65}Na_{0.36})[Si_{29.80}Al_{6.20}O_{72}]22.76H_2O$

Ferrierite fibres show high amounts of adsorbed EPR probes, suggesting an increased ability to adsorb and interact with related chemicals.



These outcomes, in agreement with Gualtieri et al. (2018), indicate that this **fibrous ferrierite should be considered a potential health hazard.**





Comparison of the interaction capability (as adsorbed percentage of probes) of the investigated fibrous zeolites (from Mattioli et al., 2016a, 2018, 2022; Cangiotti et al., 2017; Giordani et al., 2016, 2017; Gualtieri et al., 2018)

The interaction capability is very high for the carcinogenic erionite samples and is comparable with that measured for ferrierite and offretite. These zeolites exceed 95% and can be considered highly toxic to carcinogenic.

Mesolite and thomsonite show lower interaction capability (60-70 %) and can be considered harmful, while scolecite shows no interaction and can be assumed to be a non-toxic zeolite.

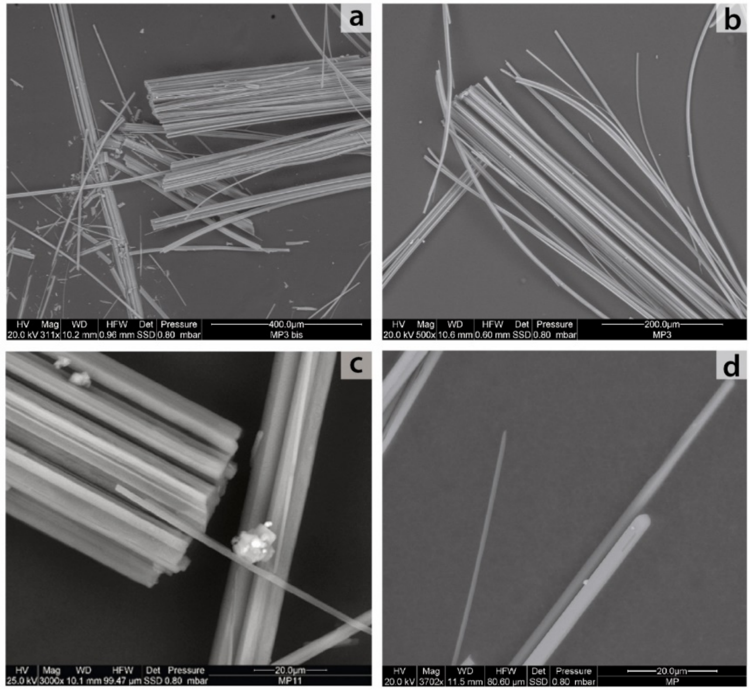
The interaction capability seems to be a very useful parameter in evaluating the toxicity of a mineral, which could also be considered in the assessment of potential health hazard calculation of the fibre potential toxicity index (FPTI) (Gualtieri, 2018).

Another contribution to the characterization of fibrous minerals is that of Giordani et al. (2022c), where a study on the **water-soluble natural epsomite fibres** from Perticara Mine (Italy) was conducted using SEM-EDS, XRPD, ICP-AES and alpha spectrometry measurements.

The morphological and morphometric results showed that most fibres are inhalable (**Dae = 5.09 µm**) and can be potentially adsorbed from all parts of the respiratory tract.

WIDTH		LENGHT	
≤3 µm	25.10%	<20 µm	13.11%
3.1–5 µm	44.40%	20–100 µm	48.03%
>5 µm	30.50%	100–200 µm	32.07%
min	0.5 µm	>200 µm	6.78%
max	22 µm	min	4.8 µm
σ	4.79	max	260 µm
		σ	63

Giordani M., Meli M.A., Roselli C., Betti M., Peruzzi, F., Taussi M., Valentini L., Fagiolino I., Mattioli M. (2022). *Could soluble minerals be hazardous to human health? Evidence from fibrous epsomite*. ENVIRONMENTAL RESEARCH, 206, 112579-112591, doi: 10.1016/j.envres.2021.112579

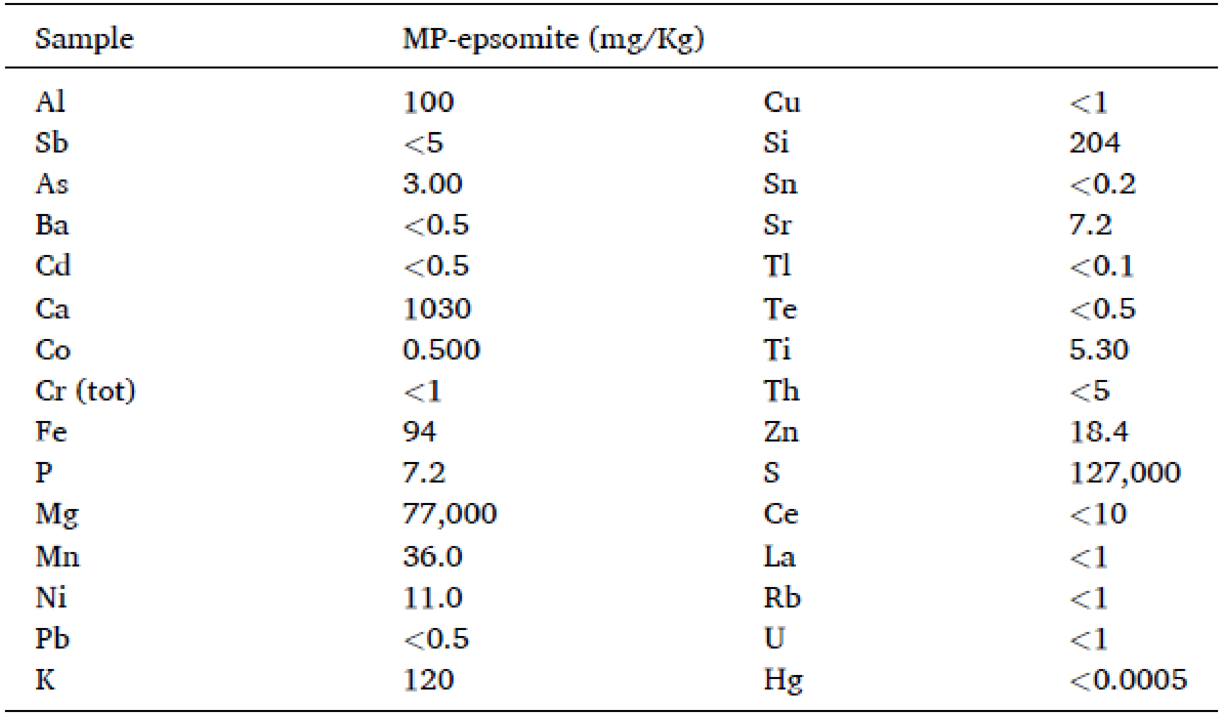


Chemical analysis reveals significant amounts of toxic elements (As, Co, Fe, Mn, Ni, Sr, Ti, Zn) and surprisingly high contents of radioactive isotopes (^{210}Po and ^{228}Th) in epsomite crystals, making the inhalation of these fibres potentially hazardous to human health.

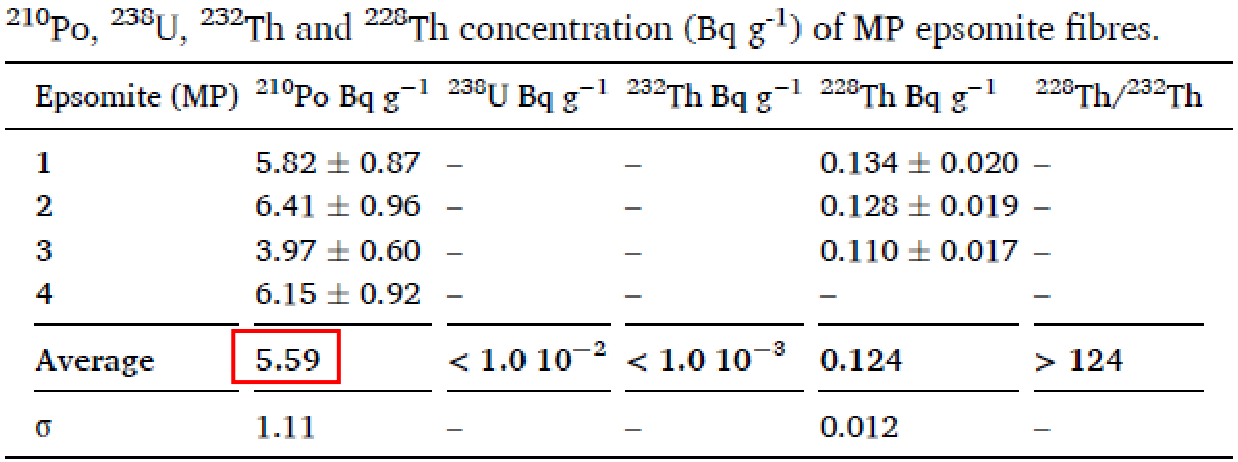
^{210}Po = 5.59 Bq/g

^{210}Po in surface soils with a normal radiation background is 0.01 – 0.2 Bq/g

This study opens a new window on soluble minerals, such as epsomite, which can be present in both natural and anthropic environments and have never been considered from the point of view of their potential hazard.



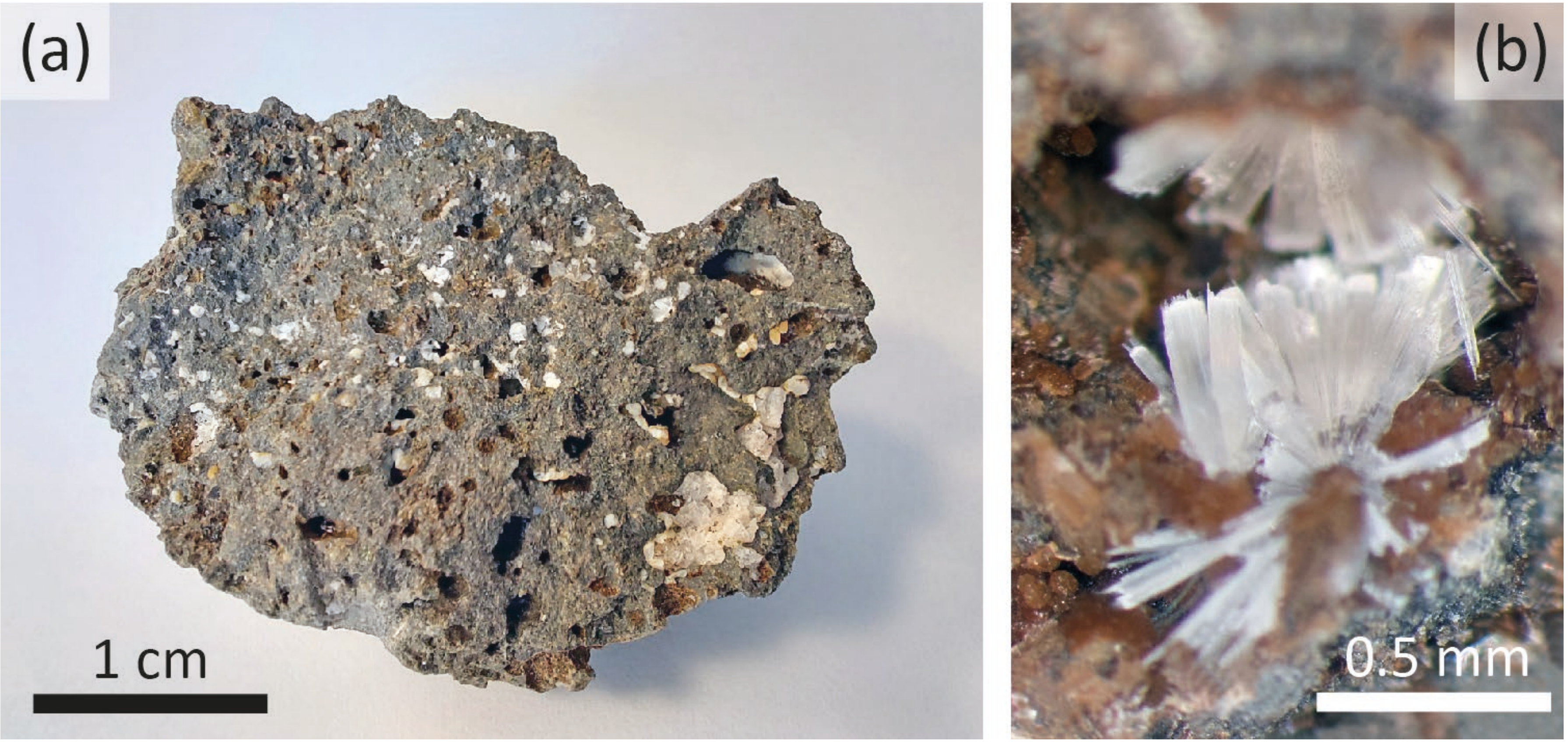
Sample	MP-epsomite (mg/Kg)		
Al	100	Cu	<1
Sb	<5	Si	204
As	3.00	Sn	<0.2
Ba	<0.5	Sr	7.2
Cd	<0.5	Tl	<0.1
Ca	1030	Te	<0.5
Co	0.500	Ti	5.30
Cr (tot)	<1	Th	<5
Fe	94	Zn	18.4
P	7.2	S	127,000
Mg	77,000	Ce	<10
Mn	36.0	La	<1
Ni	11.0	Rb	<1
Pb	<0.5	U	<1
K	120	Hg	<0.0005



^{210}Po, ^{238}U, ^{232}Th and ^{228}Th concentration (Bq g^{-1}) of MP epsomite fibres.

Epsomite (MP)	^{210}Po Bq g^{-1}	^{238}U Bq g^{-1}	^{232}Th Bq g^{-1}	^{228}Th Bq g^{-1}	^{228}Th/^{232}Th
1	5.82 ± 0.87	–	–	0.134 ± 0.020	–
2	6.41 ± 0.96	–	–	0.128 ± 0.019	–
3	3.97 ± 0.60	–	–	0.110 ± 0.017	–
4	6.15 ± 0.92	–	–	–	–
Average	5.59	$< 1.0\ 10^{-2}$	$< 1.0\ 10^{-3}$	0.124	> 124
σ	1.11	–	–	0.012	–

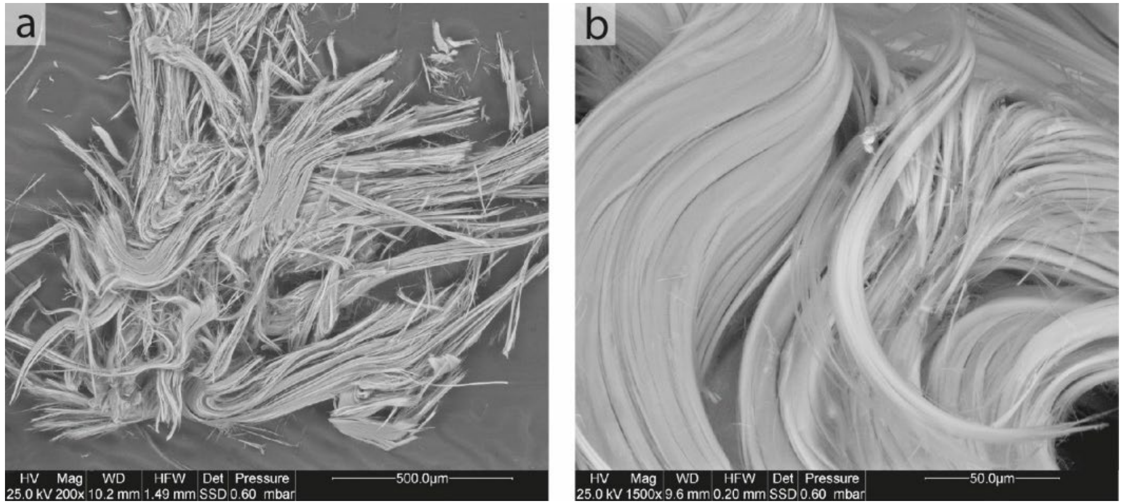
Finally, the last (but not least) work relates to the occurrence and crystal-chemical characterization of carcinogenic **fibrous erionite discovered for the first time within vesicles and vugs of the volcanic rocks of Latium, Italy**. The erionite samples were investigated using SEM, TGA, PXRD, FTIR and Raman spectroscopies.



Two coexisting different types of erionite were found, having different crystal morphologies, chemical composition, and structure.

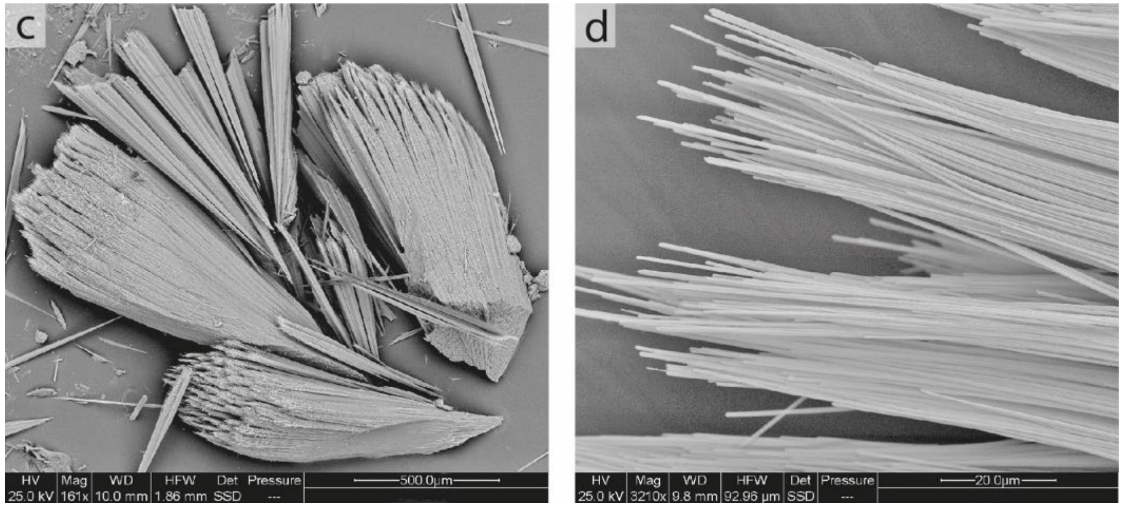
The first type is an extremely fibrous **erionite-K**, with Si/(Si+Al) ratio of 0.77, cell parameters a=13.255 Å, c=15.053 Å and cell volume V=2290.49 Å3.

$(K_{2.68}Ca_{1.86}Na_{0.96}Mg_{0.23})\ [Al_{8.19}Si_{27.81}O_{72}]\cdot 29.58\ H_2O$



The second type is acicular to highly fibrous **erionite-Na**, with a lower Si/(Si+Al) ratio (0.72-0.73) and larger cell parameters (a=13.291 Å, c=15.146 Å, cell volume V=2317.35 Å3).

$(Na_{4.82}K_{2.30}Ca_{1.08}Mg_{0.26})\ [Al_{10.05}Si_{25.95}O_{72}]\cdot 30.14\ H_2O$



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First occurrence, crystal-chemistry and structure of erionite, a carcinogenic fibrous zeolite, from the volcanic rocks of Latium (Italy)

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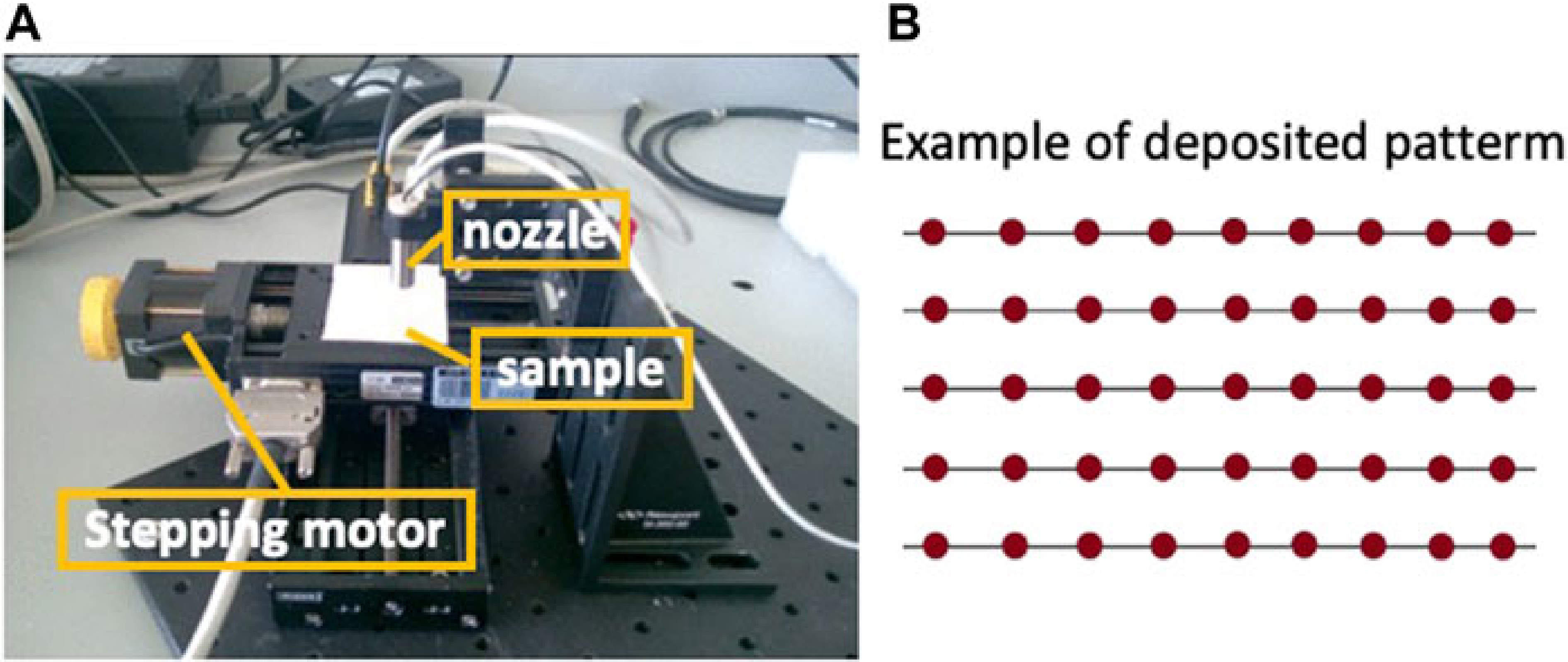
Regarding the second topic



The microdrop device **(A)** and a schematic example of droplets (red spots) deposition pattern **(B)**, where the X-Y distances can be adjusted at any values *via* the used software (see text for details).

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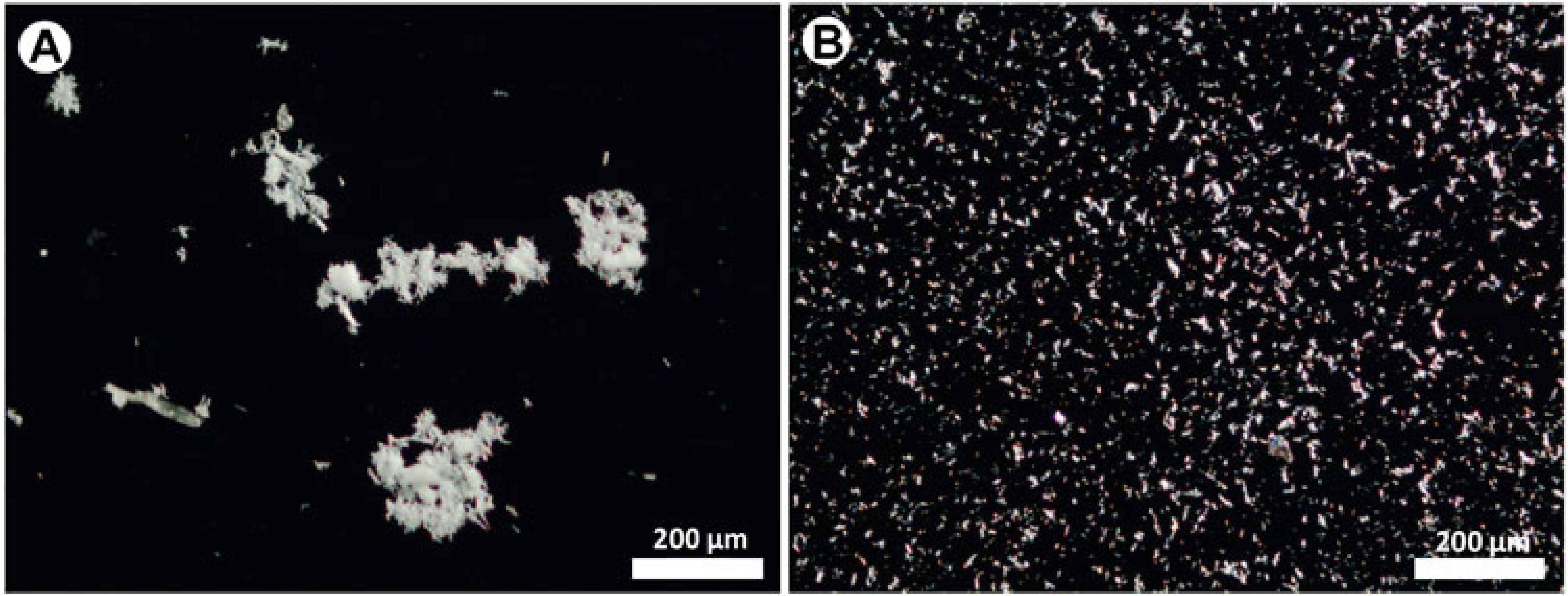

Optical images of the asbestos depositions obtained with **(A)** the pipette (drop) and **(B)** the micro-drop methods, respectively. Optical images taken with ×10 objective lens.

Regarding the second topic

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A new approach to deposit homogeneous samples of asbestos fibres for toxicological tests *in vitro*

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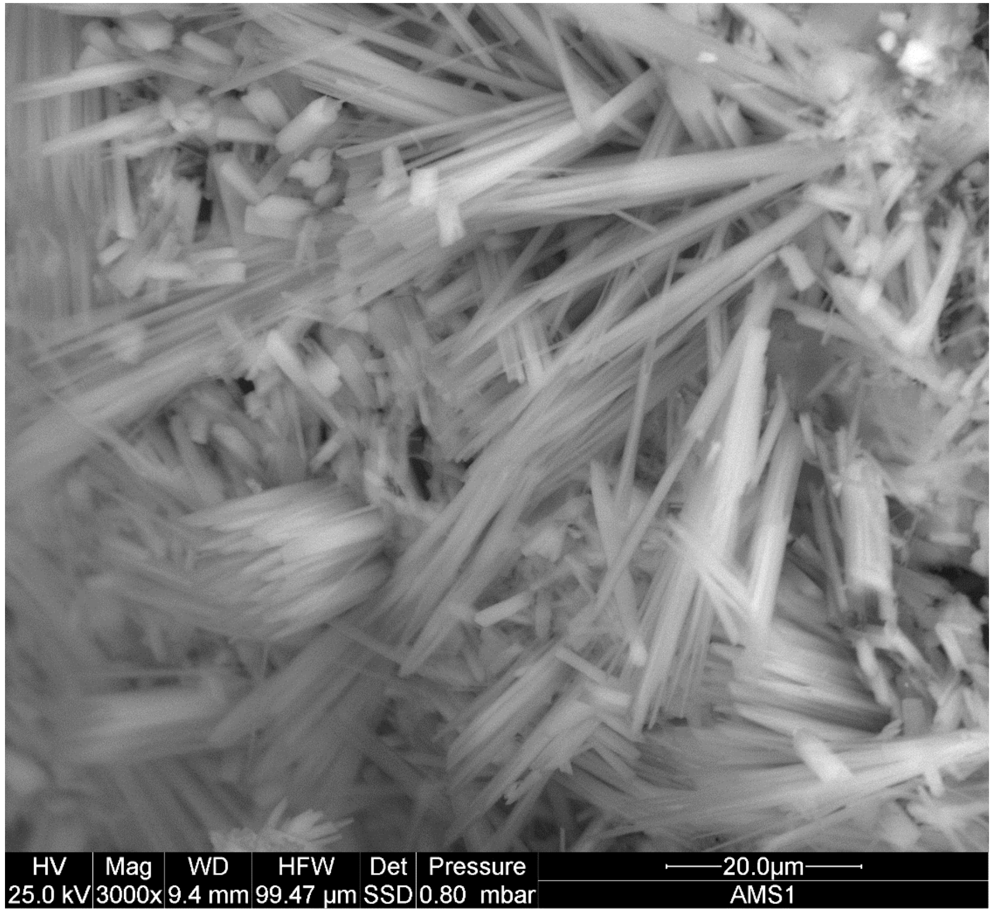

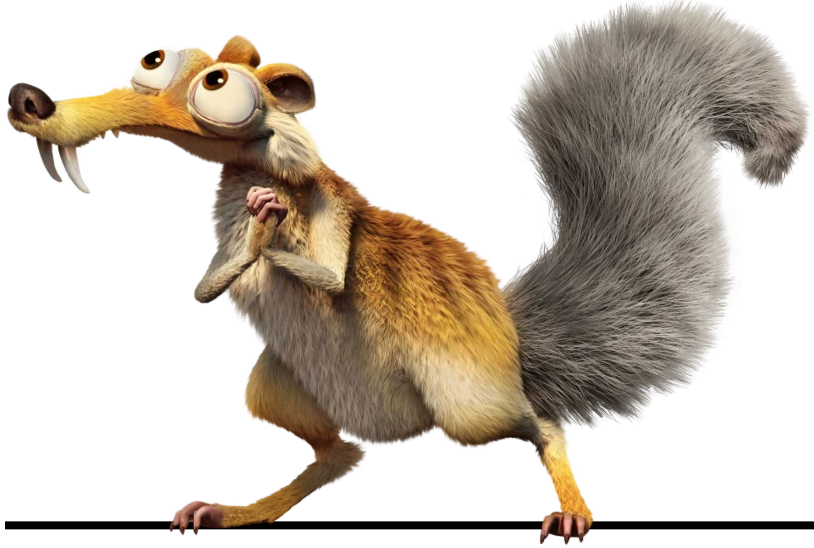

Grazie a tutti per l’attenzione