

## MINERALOGICAL STUDY OF THE FIBROUS ZEOLITES ERIONITE AND OFFRETITE AND HAZARD ASSESSMENT

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### INTRODUCTION

Several fibrous minerals are known in nature, some of them having chemical and physical characteristics very useful in various industrial processes and applications. However, some fibrous minerals are considered highly hazardous to human health, because of their capability to divide into inhalable size fibers, together with their biopersistence in the lungs. This is the case, for example, of the well-known asbestos minerals. Nevertheless, there are many other fibrous minerals with physical and chemical characteristics very similar to asbestos, which have not been sufficiently investigated. For some of them, such as attapulgite, palygorskyte, byssolite, picrolite, sepiolite, thomsonite, scolecite, mesolite, natrolite and offretite, the dangerousness has not been neither confirmed nor denied, yet. For others fibrous minerals (*e.g.*, jamesonite, carlostauranite, wollastonite, nemalite, clinoptilolite, phillipsite, mordenite) preliminary studies seem to point out some toxic effects. Lastly, other fibrous minerals have already been well studied and are currently considered carcinogenic by inhalation, such as fluoro-edenite, balangeroite, and erionite.

Several fibrous minerals belong to the zeolite group. Zeolites occur worldwide and are widely used in materials for the construction industry, in paper, in agriculture, and in other applications. Therefore, potential exposure to zeolite fibers may occur during their mining, production and use (IARC, 1997). In particular, the exposure to erionite fibers has been unambiguously linked to malignant mesothelioma (Baris *et al.*, 1978); moreover, *in vivo* studies have demonstrated that erionite is significantly more tumorigenic than asbestos (Coffin *et al.*, 1992). For these reasons, the International Agency for Research on Cancer has referred erionite as a Class 1 carcinogen, and at present it is considered as the most carcinogenic mineral (IARC, 1987, 2012). Recently, a growing concern has developed regarding the potential risks associated with environmental and occupational exposures to erionite in Turkey (Carbone *et al.*, 2011), in the United States (Saini-Eidukat & Triplett, 2014), in Mexico (Ortega-Guerrero & Carrasco-Núñez, 2014), and possibly in Iran (Ilgen *et al.*, 2015); moreover, it is very likely that this problem could also be extended to other countries in the future.

The main mechanisms by which inhaled fibers of erionite, as well as other fibrous particulates, induce pathological changes comprise the following factors: (a) physical properties of the fibrous mineral particles such as diameter, length and aspect ratio; (b) chemical-mineralogical properties (fibers type, chemical composition and surface reactivity); (c) the ability to generate reactive oxygen species (ROS); and (d) the biopersistence. Despite of the great number of researches, the relationships among mineralogical features and biological activity of erionite have not been fully understood and there are no systematic studies on the distribution of erionite or other similar fibrous zeolites in the environment. Moreover, there is another zeolite, named offretite, which is closely related both structurally and chemically to erionite. Despite commonly occurring as prisms, offretite has also been found under asbestiform habit, meaning that the morphology of its crystals has not yet been fully known and many mineralogical aspects are still to be discovered. Due to these similarities and to the possible intergrowth, the distinction between erionite and offretite can be hampered. To date, there are no studies regarding a potentially hazard of offretite fibers and it is unclear whether the mineralogical distinction between erionite and offretite has any health implications.

### THE RESEARCH PROJECT

The gap of knowledge of the fibrous zeolites erionite and offretite has been the starting point for the

development of the present PhD project. A multi-methodological approach, based on field investigation, morphological characterization, SEM/EDS chemical analysis and structure refinement through X-ray powder diffraction was applied to different samples of potentially carcinogenic erionite and offretite from Italy. These investigations were performed on representative samples with variable morphologies, ranging from prismatic, through acicular and fibrous, to extremely fibrous asbestiform habits.

Successively, morpho-chemical characterization and surface properties determinations were performed on a selection of different asbestiform zeolite fibers: two erionite samples, one offretite sample and, for comparison, one scolecite sample. These samples have been used to carry out *in-vitro* experiments to assess the level of reactivity and transformation that such fibers may induce to micelles and membranes in contact with them, and therefore, their indirect capability to trigger asbestos-related lung diseases. With this aim, specific surface area determinations coupled with EPR analysis and TEM images in the presence of model membranes have been performed. This type of study has allowed to obtain information on the fiber internalization in the membranes and on the interactions occurring at a molecular level that mimicked the attack of the fibers at the cell membrane.

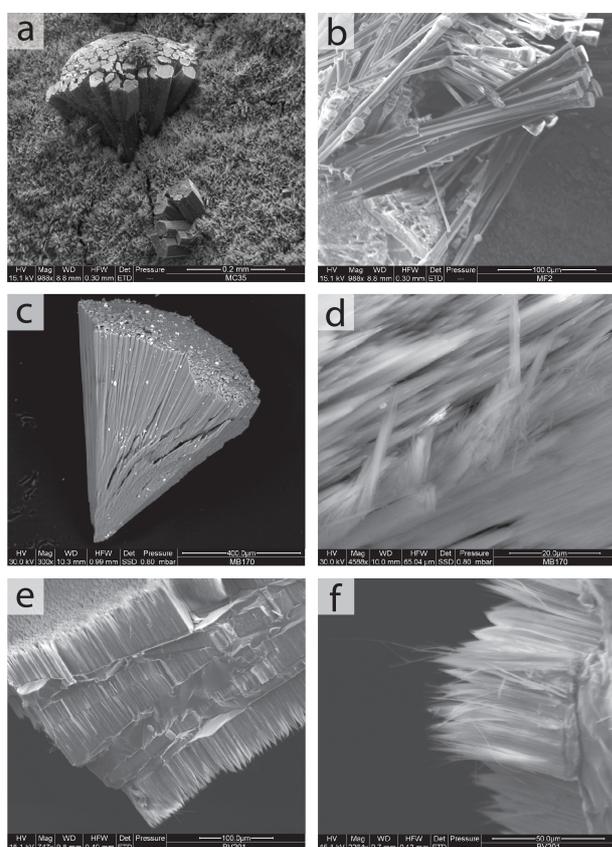


Fig. 1 - Representative SEM images of the studied samples. a) Prismatic crystals of erionite grouped in radial aggregate of millimetric size (MC35). b) Acicular erionite crystals with hexagonal section often grouped in packets of larger size (MF2). c) Acicular to very fibrous crystals of erionite grouped in radial aggregates (MB170). d) Particular of the previous sample showing a large number of small fibrils with rigid to flexible behavior (MB170). e) Typical erionite-levyne-erionite sequence forming a “sandwich-like” morphology (BV201). f) Details of the extremely fibrous habit consisting of flexible fibers with a typical woolly aspect (BV201).

## RESULTS AND DISCUSSION

### *Italian erionite*

In the first part of this study new mineralogical, structural and chemical data of 4 representative erionite samples (MC35, MF2, MB170, BV201) from Northern Italy were reported, where this carcinogenic zeolite occurs as fibers of inhalable size (Giordani *et al.*, 2016, 2017).

MC35 is an erionite-Ca characterized by prismatic habit with solid appearance, rigid behavior, and no apparent fibrous elements (Fig. 1a). MF2 is an erionite-Na characterized by acicular crystals with a great tendency to separate fibers and fibrils with rigid behavior (Fig. 1b). MB170 is an erionite-Ca showing acicular to fibrous crystals, often separating in a great number of small fibrils with rigid to flexible behavior (Fig. 1c, d). BV201 is an erionite-Ca with an extremely fibrous (hair-like) habit, with flexible appearance and a marked tendency to split up into thin fibers and fibrils (Fig. 1e, f).

From the structural point of view, MB170 is characterized by an unusual preferred partition of Al at the T1 site instead of T2 as observed in all refinements of erionite samples. A mismatch was detected between the *a*-parameter of erionite-Ca and levyne-Ca that are intergrown in sample BV201. Since the single-layer of 6-membered rings of (Si, Al)O<sub>4</sub> tetrahedra, whose stacking along the *z*-axis build both structures, is common, the mismatch produced some strain that possibly favors the curling of fibrils. As a whole, erionite is

present in 65% of the investigated outcrops, with an estimated amount varying from 10 to 40 vol.% of the total secondary minerals, which are crystallized within vugs and cavities of basaltic rocks. These amounts are not negligible for effects on human health, especially considering that these basalts often host mining or quarrying activities since these rocks are extensively used as construction material.

The discovery of fibrous erionite in the Lessini Mountains suggests the need for a detailed risk assessment in Italy, with specific studies such as a quantification of the potentially airborne fibers and targeted epidemiological surveillance. This need is even more evident if one considers that erionite, or some other fibrous zeolites, might be potentially present in many other volcanic rocks, which extensively crop out in many Italian regions (Fig. 2).

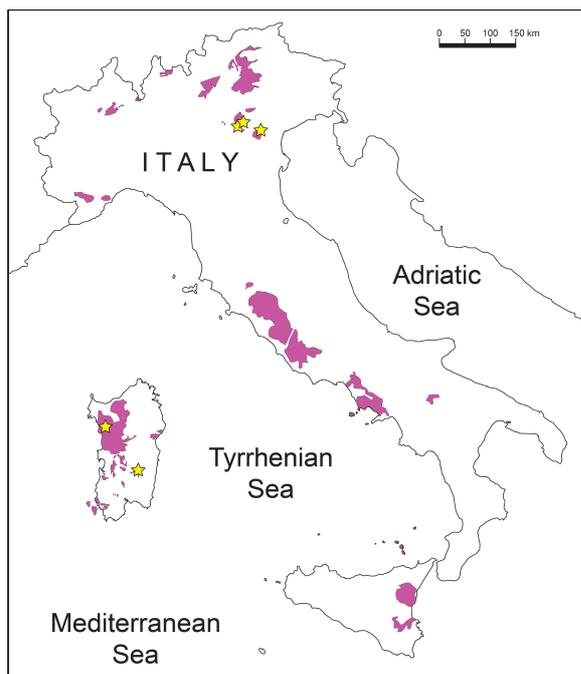


Fig. 2 - Sketch map of Italy showing the sites where erionite crystals have been described in literature (stars) and the geological distribution of the other potentially erionite-bearing volcanic rocks (purple red).

lengths up to 500  $\mu\text{m}$ , whereas the acicular variety is characterized by the same lengths but very small diameters ( $< 1 \mu\text{m}$ ). The main mode observed in the erionite fibers of MB2287 is 20-25  $\mu\text{m}$  and since  $\sim 93\%$  of the measured fibers are  $> 5 \mu\text{m}$  they may be significantly associated with carcinogenesis when breathed (Stanton *et al.*, 1981; WHO, 1986; Bernstein *et al.*, 2005). The various offretite samples showed different mechanical behavior, having an extremely fibrous habit with flexible to rigid appearance or forming prismatic to acicular, brittle crystals.

The chemical composition of the investigated offretite samples is coherent with reference data: R ranges from 0.71 to 0.74, the EF cations  $\text{K}^+$ ,  $\text{Mg}^{2+}$  and  $\text{Ca}^{2+}$  are present in all samples in comparable proportions, and  $\text{Na}^+$ ,  $\text{Sr}^{2+}$ ,  $\text{Ba}^{2+}$  and  $\text{Fe}^{2+,3+}$  are absent. However, observing the chemical data in greater detail, it can be observed that the prismatic to acicular crystals have similar compositions, with  $\text{Mg}^{2+}$  content slightly lower than  $\text{K}^+$  and  $\text{Ca}^{2+}$ ; differently, the asbestiform offretite crystals are characterized by a  $\text{Mg}^{2+}$  content which is slightly higher than that of the other EF cations.

The present study indicates that, in some lithotypes of the Northern Italy, the zeolite offretite may crystallize with asbestiform habit, becoming potentially harmful. For the above reason, the related host-rocks should be carefully checked before their use as building or construction materials and, to this aim, the role of geoscientists is crucial in guiding safe rock extraction.

Given their widespread occurrence and huge extension the possibility of an environmental exposure to hazardous fibrous zeolites related to these volcanic rocks needs to be taken seriously. These results provide the basis for health and safety protection programs and for a better scientific understanding of this carcinogenic fibrous zeolite.

#### *Italian offretite*

In the second part of this work a detailed morphological, mineralogical, and chemical characterization of different samples of offretite recently discovered in Northern Italy (some of which showing asbestiform habit and suspected to be carcinogenic) is presented. In the investigated samples, the habit of offretite varies from stocky-prismatic crystals with a solid appearance of FF102 (Fig. 3a, b) to prismatic or acicular with rigid mechanical behavior of AD13 (Fig. 3c, d), to extremely fibrous crystals (asbestiform) with rigid to flexible behavior of MB2287 (Fig. 3e, f). The prismatic and acicular crystal habits occur more commonly, whereas asbestiform habit is relatively rare. The stocky-prismatic and prismatic crystals have diameters of  $\sim 50 \mu\text{m}$  and

The present results, such as those for erionite, suggest the need of a detailed Italian mapping of natural sites characterized by the potential occurrence of offretite, but also for others fibrous minerals. Furthermore, these data can be used in order to assess the health risks related to the exposure to mineral fibers during human activities, such as road constructions, quarry excavations and farming that may induce disturbance in the fibrous minerals-bearing rocks and may trigger unplanned fibers release processes. It is relevant to note that, among the fibrous zeolites, erionite is the only one that was classified as a human carcinogen (IARC, 1987), although other

species should not be considered intrinsically safe (IARC, 1997; Stephenson *et al.*, 1999). Despite of the lack of epidemiological information on populations exposed to natural asbestiform minerals other than asbestos and erionite, results acquired in the present investigation suggest that other mineral fibers of similar size, habit, and biopersistence may carry a risk for humans.

#### *Surface properties determinations and in-vitro experiments*

The third part of this study consist of a combined approach of morphological, mineralogical, chemical, and surface characterization of the four asbestiform zeolites termed GF1, MD8 (erionite from USA and Turkey respectively), BV12 (offretite from Italy), and for comparison SC1 (scolecite, from India), coupled with reactivity studies by means of spin probes, that has proved to be very helpful to shed new light on the surface properties and interacting ability of these materials which are very likely related to their eventual carcinogenicity.

First, a detailed view of the morphology, chemical compositions and surface characterization (BET) of these representative samples have been obtained (Table 1). The chemical, morphological and BET characterization indicated an extremely fibrous, hair-like structure for the carcinogenic erionite-K GF1, which was rich in  $K^+$  and  $Ca^{2+}$ , and characterized by a relatively high surface area (Mattioli *et al.*, 2016). The MD8 sample, compared to GF1, was less rich in  $Ca^{2+}$ , and less homogeneous in structure since it was

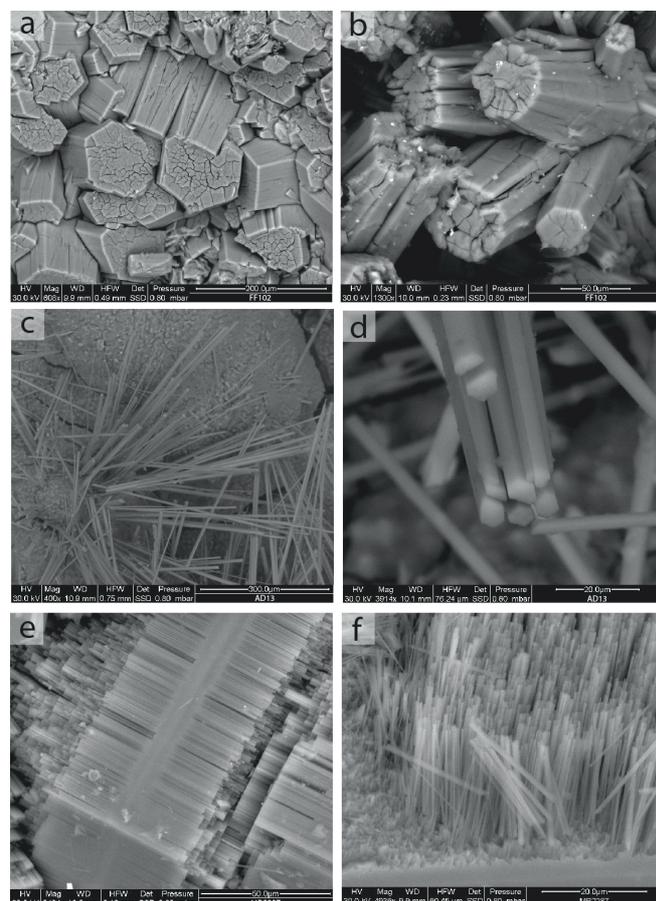


Fig. 3 - Representative SEM images of the studied samples. a) Stocky-prismatic crystals of offretite with hexagonal section (FF102). b) Radial aggregates of offretite prisms, characterized by evident fractures (FF102). c) Very elongated, acicular to fibrous offretite crystals grouped in radial aggregates with rigid to flexible behavior (AD13). d) Particular of the previous sample showing the thin diameter of hexagonal offretite fibrils (AD13). e) Offretite-chabasite-offretite sequence forming a sandwich-like morphology (MB2287). f) Details of the parallel growth of the extremely fibrous (asbestiform) offretite consisting of rigid to flexible thin fibers and fibrils (MB2287).

characterized by well-developed, acicular to fibrous erionite-K crystals. It also had a lower surface area than GF1. The offretite BV12 sample showed a further decrease in surface area if compared to the erionite samples, but the number of its small pores (interstices among fibers aggregates) increased at the expense of the large ones. However, BV12 and MD8 resulted quite similar in structure, being the former constituted by elongated fibers often grouped in roughly prismatic forms. Chemically, the offretite was characterized by a relatively high

amount of  $Mg^{2+}$ , but also MD8 showed some Mg-rich zones which were absent in GF1. The zeolite sample SC1 was almost non fibrous and its surface area resulted the smallest. It was characterized by large pores, *i.e.*, open windows in the zeolite-fibers aggregates, and  $Ca^{2+}$ . Therefore, it showed significantly different chemical and morphological properties with respect to the erionite and offretite fibrous zeolites.

Table 1 - Average chemical compositions and surface areas, obtained by the EPMA and BET methods, respectively, of the zeolite fibers investigated in this study

Sample	Zeolite family	Average chemical composition	Surface Area (m <sup>2</sup> /g)
GF1	Erionite	$K_{2.56}Ca_{1.72}Na_{0.74}Mg_{0.35}[Al_{8.08}Si_{28.05}O_{72}] \cdot 29.54H_2O$	22.3
MD8	Erionite	$K_{3.46}Na_{2.38}Ca_{0.98}Mg_{0.16}[Al_{7.94}Si_{28}O_{72}] \cdot 32.31H_2O$	15.4
BV12	Offretite	$K_{2.06}Mg_{1.67}Ca_{1.17}[Al_{7.61}Si_{28.14}O_{72}] \cdot 31.03H_2O$	9.92
SC1	Scolecite	$Ca_{5.86}[Al_{14.35}Si_{22.31}O_{80}] \cdot 21.12H_2O$	1.5

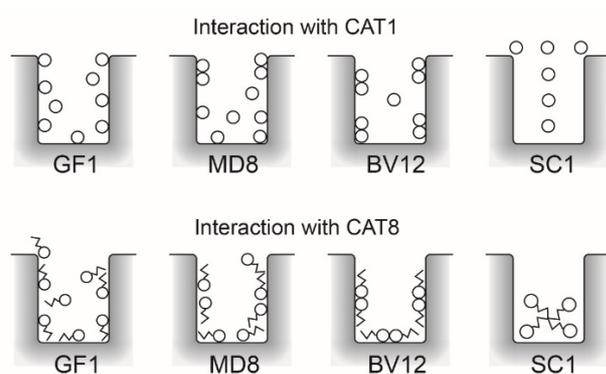


Fig. 4 - Graphical summary of the interaction modes of CAT1 and CAT8 onto the zeolite surface, as obtained from the EPR analysis.

Useful information about the interacting ability of the different zeolites were obtained by means of the EPR study using CAT1 and CAT8 as spin probes. These information were related to the morphology and BET characterization of the zeolites. The EPR results about the adsorption mechanism of the spin probes onto the four different zeolites are graphically summarized in Figure 4. In detail, GF1 surface binds the positively charged CAT group at polar/charged interacting sites which are well distributed, intercalated by less polar sites (Si-O-Si) which are interacting with the hydrophobic part of the probes. MD8 surface is less homogeneous and the polar/charged sites are closer to each other than in

case of GF1. This provokes a stronger binding, but also some spin-spin interactions between the nitroxide groups in close positions.

The interacting ability of offretite BV12 surface is much lower than that found for the erionite samples, mainly GF1: the probes interacting with BV12 are mainly trapped in small pores created in the fibers aggregates and spin-spin interactions are favoured. However, the interacting ability of BV12 is much higher than that of SC1. For this non-fibrous and non-carcinogenic zeolite, the adsorption is poor and the few adsorbed CAT1 radicals are free whereas CAT8 radicals self-aggregate and poorly interact.

These results help to clarify the surface interacting properties of the erionite and offretite fibrous zeolites that may be related to the eventual carcinogenicity of these zeolite fibers.

The same selection of asbestiform zeolite fibers was also studied by analyzing the electron paramagnetic resonance (EPR) spectra of selected surfactant spin probes and by TEM images in the presence of model membranes (cetyltrimethylammonium (CTAB) micelles, egg-lecithin liposomes, and dimyristoylphosphatidylcholine (DMPC) liposomes) to get information on the fibers internalization in the membranes and the interactions occurring at a molecular level that mimicked the attack of the fibers at the cell membrane. The spin-probe EPR and TEM study demonstrated the internalization of the fibers into the

aggregates and clarified both the structure organization of the fiber-containing aggregates and the interactions occurring at a molecular level (Cangiotti *et al.*, 2017). For the CTAB micelles both the spin probes, CAT16 and 5DSA, provided information on structure and interactions by means of a computer aided EPR analysis. The adsorbed percentage for the various zeolites follows the series GF1 > MD8 > BV12 > SC1 in line with the decrease in surface area evaluated using BET method. In this case, it is the external surface area that makes the difference.

EPR parameters indicate that GF1 particles enter the CTAB micelles in the supernatant suspension and modify their structure towards a bilayer like organization, as also shown by TEM analysis (Fig. 5b-d), but GF1 fibers do not destroy the micelles. In the filtered solid, the micelles seem to well integrate with the zeolite particles being affected in their structure. 70% of the micelles form a double-layer organization of the surfactants, whereas 30% of the micelles are squeezed in restricted space in the fiber-aggregates porosities. Definitely, GF1 is better entering the membrane structure if compared to the other zeolites. Conversely, BV12 offretite particles partially destroy the micelle structure when entering the micelles in suspension but a fraction of micelles is hosting the fibers with a relatively smaller structural variation with respect to GF1, as also shown by TEM images (Fig. 5e, f). Also in the filtered BV12 solid, the micelles partially destructurate and partially host the BV12 fibers. MD8 behaviour in suspension is intermediate between GF1 and BV12, but quite similar to BV12 for the structural variations, as indicated by TEM analysis (Fig. 5g, h); in the filtered BV12 solid, the

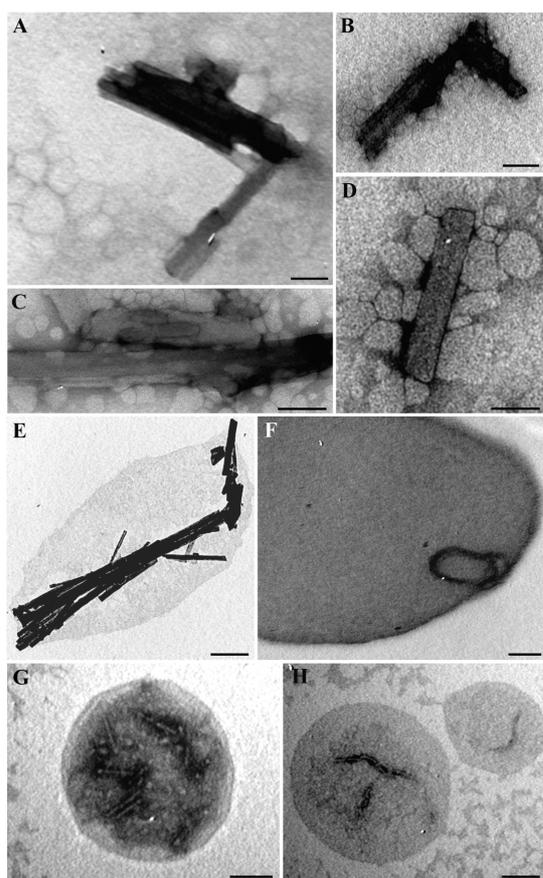


Figure 5. TEM images of SC1 (A), GF1 (B-D), BV12 (E, F) MD8 (G, H) zeolites internalized by the micelles. Bars: 50 nm (92000x) for A, B, D; 100 nm for C (130000x), G, H (62000x); 200 nm for E (32000x) and F (62000x).

micelles are squeezed and destructurate without forming the ordered layer found for GF1 and the surfactant heads go to interact with the zeolite surface. SC1 is poorly interacting with the micelles, even if a small internalization occurs as also demonstrated by TEM (Fig. 5a). SC1 particles poorly affect the micellar structure even in the filtered-solid sample, and a low amount of adsorbed micelles is squeezed in the interstices of SC1 solid-particle aggregates. For the lecithin liposomes, only 5DSA could be used as a probe, whereas CAT16 is poorly entering the liposomes and not considered. The modifications induced by GF1 fibers on the liposome structure are mainly due to interactions at the liposome interfaces, without perturbing the order. The fibers do not destroy the membrane, but are probably able to cross the liposome and enter inside the core solution. For MD8 and BV12, the probe environment strongly changes due to the insertion of these fibers into the liposome bilayer. Therefore, we suppose that the fibers remain into the lecithin liposomes and do not cross the membrane to go inside. Indeed, the structure of the liposomes in the filtered solids strongly changes due to liposome squeezing in the fiber aggregates. The liposomes only slightly interact with SC1 that is poorly changing the liposome structure in suspension with respect to the liposomes in the absence of the fibers.

GF1 fibers are selectively internalized into DMPC liposomes also changing their structure which becomes more rigid and ordered, and also more

permeable to the surfactant probe. In this case the fibers do not cross the membrane, but remain inside it changing the structure. A smaller structural variation was found for MD8 and BV12 if compared to GF1, as found for the micelles. The SC1 fibers are poorly included in DMPC liposomes and work as a barrier, which impedes to the apolar probes to enter the liposome structure.

The carcinogenicity of the zeolites, hypothesized in the series SC1 < BV12 < MD8 < GF1, may be correlated to an increased destructure of the membrane. The results from the filtered solids are in line with this expectations indicating, for the series above, the formation of a membrane structure which is progressively less squeezed in the fiber-aggregate porosities, more polar, and more ordered in the filtered solid.

This study is therefore helpful in clarifying the structural modifications and the interactions occurring when model membranes are in contact with asbestiform zeolite fibers, which are known or suspected to be carcinogenic. Of course the model membranes constitute a simplified system to investigate the action of the carcinogenic fibers on lung and mesothelial cell membranes to cause mesothelioma cancer disease. We may try to extrapolate the information of these simplified systems onto the true ones really involved in the pathology, but, in light of the obtained results, we are investigating by EPR and TEM the systems constituted by the erionite and offretite fibers in cell dispersions.

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