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SOFTWARE ARTICLE

WebFPTI: A tool to predict the toxicity/pathogenicity of mineral fibres including asbestos

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Abstract
The risk assessment for the human health of airborne mineral fibres, including asbestos minerals, is a complex task. WebFPTI is a browser-based software written in Python that allows users to calculate an index of toxicity and pathogenicity potential of mineral fibres based on their crystal-chemical-physical properties. WebFPTI can be a powerful tool for both academy and environmental/health institutions to classify the carcinogenicity potential of (respirable) mineral fibres, so that specific actions aimed at protecting workers and general public can be fostered.

Keywords Mineral fibres · Toxicity · Pathogenicity · Python

Introduction

Mineral fibres are ubiquitous on the Earth and count more than 400 mineral species that display a fibrous or fibrous-asbestiform crystal habit (Belluso et al. 2017). Asbestos minerals, fibrous erionite zeolite and fibrous fluoro-edenite amphibole are universally known mineral fibres that represent a recognised health hazard (IARC 2012, 2017). Asbestos is a commercial term used to identify the fibrous-asbestiform variety of six minerals: chrysotile (serpentine asbestos) and five amphiboles, i.e., actinolite asbestos, amosite (asbestos cummingtonite-grunerite), anthophyllite asbestos, crocidolite (asbestos riebeckite) and tremolite asbestos (IARC 2012). Since the mid-50s, epidemiologic and carcinogenicity studies have provided robust scientific evidence that all six asbestos types, if inhaled, may induce lung diseases of various nature (namely asbestosis, lung cancer and malignant mesothelioma) (IARC 2012). Consequently, the International Agency for Research on Cancer (IARC) included the six asbestos minerals in *Group 1* "substance carcinogenic to humans". Fibrous erionite and fibrous fluoro-edenite are responsible for mesothelioma epidemics in some villages of Central Cappadocia (Turkey) and east Sicily (Italy), respectively (Comba et al. 2003; Carbone et al. 2007). In these villages, houses were built with erionite or fluoro-edenite bearing rocks and the high incidence of mesothelioma in the population was ascribed to the exposure to these airborne mineral fibres released from the building rocks (Comba et al. 2003; Carbone et al. 2007). Now erionite and fluoro-edenite are also classified as carcinogenic to humans by the IARC (IARC 2012, 2017).

Because mineral fibres naturally occur in several rocks, sediments and soils in many areas of the world, potential exposure for the population to respirable mineral dust is expected (Hamade et al. 2015). Many mineral fibres, with structure and physical/chemical properties similar to asbestos, are unclassified to date but are assumed to display the same cyto- and genotoxicity and pathogenicity potential of carcinogenic fibres. Consequently, the identification and classification of these mineral fibres is now a prime objective for many organizations/institutions that supervise the safety of public health (IARC 2012; Gualtieri 2018). In particular, these public organizations seek for tools to identify and quantify the risks associated to airborne fibres and develop management plans to minimise the risk of exposure for the general public.

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The current IARC classification is based on epidemiological and carcinogenicity studies. According to the IARC guidelines, an agent (e.g., a mineral fibre) is defined as ’carcinogenic’ if there is enough evidence (from epidemiological surveys and in vivo and in vitro studies) that it is capable of increasing the incidence of malignant neoplasms, reducing their latency, or increasing their severity or multiplicity (IARC 2012). Although the IARC evaluations are recognised worldwide, several examples of models for assessing the pathogenicity potential of asbestos and mineral fibres have emerged in the scientific literature. The best known and most used model is certainly the “fibre pathogenicity paradigm”. Developed in the 1970s-80s the fibre paradigm enables the prediction of the pathogenicity of mineral fibres depending on their length, thickness and biopersistence (Donaldson et al. 2010). According to this model, only sufficiently long (> 5 µm), thin (< 3 µm) and biopersistent fibres deposited in the lungs can cause oxidative stress, inflammation and carcinogenesis. Another noteworthy example is the mathematical exposure–response model for lung cancer and mesothelioma developed by the US Environmental Protection Agency (Nicholson 1986), subsequently modified by Berman and Crump (2008), for which the estimate of the potency of asbestos fibres to cause lung cancer is calculated by considering: the cumulative years of exposure, the average fibre concentration in the air, lengths, widths, and mineral types of asbestos fibres.

Despite a number of studies are currently planned or underway on modelling the pathogenicity potential of asbestos and asbestos-like minerals, to date there is no quantitative tool to predict a priori the health risk associated with unclassified mineral fibres. To fill this gap, Gualtieri (2018) recently proposed a quantitative predictive model of toxicity/pathogenicity of minerals fibres based on the physical/chemical and morphological parameters, inducing biochemical mechanisms responsible for in vivo adverse effects. This model delivers an index for mineral fibres (FPTI) aimed at ranking their toxicity and pathogenicity (Gualtieri et al. 2017; Gualtieri 2018).

To calculate the FPTI index of a mineral fibre, the model considers morphometric, chemical, biodurability related, and surface parameters of mineral fibres that affect their toxicity and pathogenicity upon inhalation (Gualtieri 2018). Although a complete description of the parameters is found in Gualtieri et al. (2017) and Gualtieri (2018), each parameter reported in Table 1 is shortly described hereby. The length and width of mineral fibres are key factors in toxicity, inflammation and pathogenicity of mineral fibres (Stanton et al. 1981; Churg 1993; Donaldson et al. 2010), while the curvature of the surface of the fibres affects the binding process of proteins and influence cell adhesion (Churg 1993; Lynch and Dawson 2008; Deng et al. 2012). The crystal habit of a fibre influences its depositional pathway in the respiratory tract (Gualtieri et al. 2017) while the density determines its aerodynamic diameter D_{ae} (Gualtieri et al. 2017) and therefore it affects the deposition depth of inhaled fibre in the airways (Gualtieri et al. 2017). The hydrophobic character of a fibre rules the interaction with biopolymers (i.e., proteins) and phagocytic cells (Gualtieri et al. 2017) while the surface area affects the dissolution kinetics and biodurability, the resistance to chemical/biochemical alteration (Gualtieri et al. 2017, 2018). Iron is key chemical factor (Gualtieri et al. 2017, 2019a). Fe^{2+} found at the surface of mineral fibres promotes the formation of the reactive oxygen species (ROS), with cyto- and genotoxic effects (Gualtieri et al. 2019a). To be active, iron sites must occur at the surface of the fibre in contact with the cell or cell medium. Reactivity of iron is also related to its nuclearity (i.e., the number of iron atoms joined in a single coordination entity by bridging ligands) (Gualtieri et al. 2017, 2019a). Metals other than iron prompt inflammation activity in vivo (Gualtieri et al. 2019b). Dissolution rate of a fibre is a milestone of the fibre paradigm (Donaldson et al. 2010; Gualtieri et al. 2018) because if a fibre rapidly dissolves in lung fluids (i.e., low biodurability), it is assumed to have a low biopersistence and in principle is less toxic than a fibre with high biodurability (Gualtieri et al. 2017, 2018). The rate of dissolution of iron, silica and metals controls the release into the extracellular space of substances that may generate the reactive oxygen species (ROS) (Gualtieri et al. 2017, 2019a). The electric charges surrounding the fibres, measured as ζ potential, may correlate with a number of phenomena responsible for adverse effects (e.g., hemolysis, cross-talk phenomena and apoptosis) (Pollastri et al. 2014). ζ potential also influences the agglomeration of the fibres (Pollastri et al. 2014). Fibrous zeolites may release or exchange cations in vivo, interfering with cell life cycles (Ballirano and Cametti 2015; Gualtieri 2018).

A score is assigned to each parameter, depending on its susceptibility in inducing adverse effects (Table 1). Because the parameters of the model can correlate with each other, a hierarchical scheme that considers cross-correlations has to be applied (Gualtieri 2018). A weighing scheme is associated with each parameter of the model according to its step/hierarchy H where $W_1 = 1/H$ with $H = 1$, 2 or 3. A weight defined as $W_2 = 1/U$ is also applied to each parameter of the model (Table 1). It accounts for the uncertainty in the determination of a specific parameter (n, m) and is defined by the penalty parameter U (1 = low to null uncertainty, 2 = some degree of uncertainty, 3 = high uncertainty). Hence, the $FPTI_i$ of each fibre is calculated according to the equation (Gualtieri 2018): $\mathbf{FPTI_i} = \sum_{i=1}^{n} \mathbf{W_1 \bullet W_2 \bullet T_i}$, with T_i = class value of the parameter i of the model; $W_1 = 1/H$ weight of the parameter according to its hierarchy H; $W_2 = 1/U$

Table 1 Parameters considered in the FPTI model, the values of H (hierarchy) and U (uncertainty) associated to each parameter of the FPTI model and the classes and relative weighing score associated to each parameter of the FPTI model

Parameter	H	U	Classes	Normalised score $FPTI_i$
Morphometric				
Length	1	1	> 5 µm and < 10 µm	0.1
			> 10 µm and < 20 µm	0.2
			> 20 µm	0.4
Diameter	1	1	> 1 µm and < 3 µm	0.1
			> 0.25 µm and < 1 µm	0.2
			> 0.25 µm	0.4
Crystal curvature	1	2	Flat surface (perfect crystal)	0.05
			Altered surface	0.1
			Cylindrical surface	0.2
Crystal habit	1	1	Curled	0.1
			Mixed curled/acicular	0.2
			Acicular	0.4
Fibre density	2	1	< 2.75 g/cm^3	0.05
			> 2.75 and < 3.5 g/cm^3	0.1
			> 3.5 g/cm^3	0.2
Hydrophobic character of the surface	2	1	Hydrophobic	0.05
			Amphiphilic	0.1
			Hydrophilic	0.2
Surface area	2	1	> 25 m^2/g	0.05
			< 25 and > 5 m^2/g	0.1
			< 5 m^2/g	0.2
Chemical				
Total iron content	1	2	$Fe_2O_3 + FeO$ wt% < 1	0.05
			$1 < Fe_2O_3 + FeO$ wt% < 10	0.1
			$Fe_2O_3 + FeO$ wt% > 10	0.2
Ferrous iron content	2	1	$0 < FeO$ wt% < 0.25	0.05
			0.25 < Fe Owt% < 1	0.1
			Fe Owt% > 1	0.2
Surface ferrous iron/iron nuclearity	3	2	Fe^{2+} nuclearity > 2	0.02
			Fe^{2+} nuclearity $= 2$	0.03
			Fe^{2+} nuclearity $= 1$	0.07
Content of metals other than iron*	1	1	$\sum_i \frac{C_i}{L_i} < 1$	0.1
			$1 < \sum_i \frac{C_i}{L_i} < 5$	0.2
			$\sum_i \frac{C_i}{L_i} > 5$	0.4
Biodurability related				
Dissolution rate log(R)**	2	1	< 1y	0.05
			> 1 and < 40y	0.1
			> 40y	0.2
Velocity of iron release***	3	1	< 0.1	0.03
			> 0.1 and < 1	0.07
			> 1	0.13
Velocity of silica dissolution****	3	2	< 0.5	0.02
			> 0.5 and < 1	0.03
			> 1	0.07
Velocity of release of metals*****	3	1	< 1	0.03
			> 1 and < 10	0.07
			> 10	0.13

Table 1 (continued)

Parameter	H	U	Classes	Normalised score $FPTI_i$
Surface activity				
ζ potential	1	2	Negative at pH = 4.5	0.1
			Negative at both pH = 4.5 and 7	0.2
Fibres' aggregation	3	1	$\zeta > \|20\|$	0.03
			$\|10\| < \zeta < \|20\|$	0.07
			$\|0\| < \zeta < \|10\|$	0.13
Cation exchange in zeolites	1	3	Cation Exchange	0.07
			No cation exchange	0

* = sum of the concentrations of heavy metals (Sb, As, Hg, Cd, Co, Cr, Cu, Pb, Ni, Zn, V, Be) C_i in the fibre (ppm) divided by the limit L_i for that metal according to the existing regulatory system (Gualtieri 2018); **the total dissolution time of the fibre calculated in years (y) following the standardized acellular in vitro dissolution model at pH = 4.5 described in reference Gualtieri et al. (2018); ***total content of elemental iron in the fibre (wt%) possibly made available as active iron at the surface of the fibre divided by the total dissolution time (y) of the fibre; ****total content of Si of the fibre (wt%) divided by the total dissolution time (y) of the fibre; *****total content (ppm) of heavy metals (Sb, As, Hg, Cd, Co, Cr, Cu, Pb, Ni, Zn, V, Be; Mn, Be) divided by the total dissolution time (y) of the fibre

weight of the parameter according to the uncertainty U of its determination. Table 1 also reports the classes of score assigned to each parameter $FPTI_i$.

The goal of this work is to deliver an overview of WebFPTI, an especially developed tool for the calculation of the FPTI index. WebFPTI is a browser-based tool written in Python that allows the user to assess the potential toxicity/pathogenicity of any mineral fibre. Thanks to its basic interface, WebFPTI allows the operator to insert the parameters needed to calculate the FPTI index, include them in a database for comparison with other fibres, positive and negative controls.

Software description

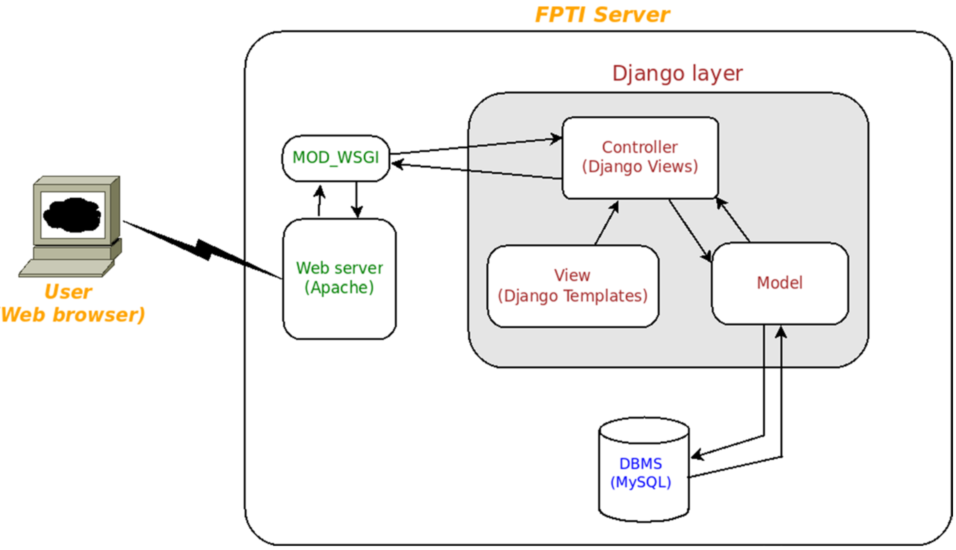
Software architecture

WebFPTI is a web-based application structured as a classical three-tier architecture. WebFPTI has been developed (and currently runs) under a Debian GNU Linux OS, but can be easily ported under any *nix operating system. The three key software components of WebFPTI are (see Fig. 1): (1) the Django highly productive framework for building and maintaining web applications, which adopts the Model-View-Controller (MVC) architectural pattern, (2) the Apache Web server with the mod_wsgi module to access Python applications, and (3) the relational database server (DBMS) MySQL to store all the relevant data (both application-specific and system data). Python/Django was chosen instead of PHP tecnology because it allowed us to reduce development time and made application maintenance easier.

Users interact with the WebFPTI server through a Graphical User Interface (GUI) presented by web browsers. The role of the various components can be best described by means of an example. Suppose a user wants to retrieve, say, the values of the parameters and the FPTI index of a give material. With reference to the above figure, the whole process runs as follows.

1. The user submits a query using some of the GUI controls, e.g., a menu and/or a button. The actual query takes the form (which is normally hidden to the user) of an HTTP request composed of a URL and possibly some additional parameters;
2. On the server, the HTTP request is handled by Apache and sent, via the mod_wsgi module, to the appropriate Django view (a Python function). The actual function that is invoked depends on the URL submitted;
3. In this particular case, the user query requires a database access. The view thus retrieves the data by interacting with the Django model component. The latter provides an abstraction over the specific DBMS adopted (hiding the particular data organization);
4. The model component performs the actual query to the DBMS and returns the results to the view according to a standard format;
5. The view "prepares" the page to be served to the user in response to the query. This is typically done by incorporating the data received by the DBMS with some HTML template (i.e., an HTML page that includes both structure and style information although missing some specific variable data). In this particular example, the view also performs the computations to evaluate the FPTI index of the particular material as a function of the parameter values retrieved by the DBMS;

Fig. 1 Components of WebFPTI



6. Finally, the complete HTML page is sent back to Apache and served to the remote user as a response to the HTTP request.

Software functionalities

WebFPTI is a software tool designed to support collaborative research endeavours to assess the toxicity and possible pathogenicity of as many fibres as possible. These first principles imply almost naturally three categories of users and, consequently, three different sets of functionalities.

Generic users

A typical "generic" user may be a professional (e.g., an industrial hygienist) who is interested in assessing the toxicity/pathogenicity potential of a mineral fibre that can be source of environmental exposure for the general public in a specific area. Another example can be an attorney involved in an asbestos related litigation who needs quantitative data on the toxicity of a specific asbestos species. To these users, WebFPTI will represent a readily-available and easy-to-use tool for preliminary assessment and comparative studies. A generic user may access the full WebFPTI database, taking advantage of the following *functionalities*:

a) listing all materials;
b) inspecting the features of a given material (i.e., the values of the chemical/physical parameters assigned to that material);
c) consult possible human annotations and the related bibliography;
d) compute and compare the FPTI index of various materials.

Contributing users

Contributing users are typically researchers and professionals working in this field (e.g., mineralogists, chemists, geologists, toxicologists) who are granted to access the WebFPTI to insert new materials. Specifically, a contributing user may perform the following actions (in addition to those allowed to generic users):

e) Insert a new material (inserting parameter data, annotation and bibliography);
f) Edit and possibly delete materials previously inserted by the same user.

Coordinator

The coordinator is in charge of supervising the scientific content available in WebFPTI. The coordinator can perform all the basic actions granted to generic and contributing users (a to f) and:

g) Review and validate the materials inserted by the contributing users. This corresponds to a "scientific endorsement" that the relevant data have rigorously been tested. Materials approved by the coordinator cannot be further edited (nor deleted) by contributing users;
h) Edit/delete consolidated materials.

Super user

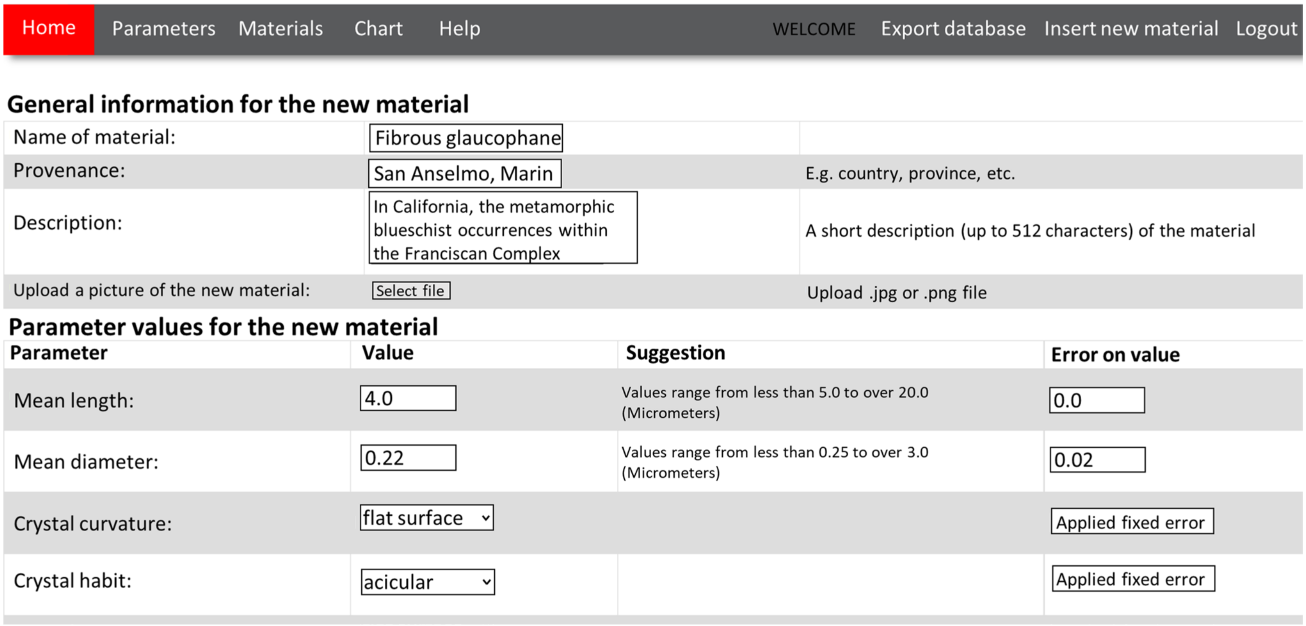
Super user is an account used for system administration involved the management and security activities. Specifically:

i) User-related administering activities, such as adding user and resetting passwords;
ii) Data management activities, such as backup and restore the WebFPTI database;
iii) Insert new parameters, edit and delete consolidated parameters.

Illustrative example

How to calculate the FPTI index of a mineral fibre

The user (e.g., Contributing users) can access the WebFPTI application via the URL: http://fibers-fpti.unimore.it. Upon successful authentication, the user will be redirected to the home page. Selecting the menu option "Insert new material", the user starts the procedure to calculate the FPTI index of a mineral fibre (Fig. 2). Operating from top to bottom, the user enters in the dialog boxes, the general information of the new material (e.g., a brief description of the material and its image), the values of each FPTI parameter (mean length, mean diameter, crystal curvature, crystal habit, fibre density, hydrophobic character of the surface, surface area, total iron content, ferrous iron, surface ferrous/iron nuclearity, content of toxic elements other than iron, fibre dissolution rate, mean velocity of iron release, velocity of amorphous silica release, mean velocity release of toxic elements, ζ potential, fibre aggregation, and cation exchange capacity) and the associated error (Fig. 2). Next to the dialog boxes, some tips help users enter the correct parameter value (Fig. 2). In the "Parameters" section, the user can find the value classes of each parameter of the FPTI index and the associated weighing score (Table 1). The FTPI index, index error, and the image of the new material (and materials already stored in the WebFPTI) are reported in the "Material" section (Fig. 3). Choosing the menu option "Chart", a histogram can be generated to compare the FPTI values of each material present in the WebFPTI database (Fig. 4). The histogram depicts the fibres with FPTI values greater than 3.00 in black, the fibres with FPTI between 2.00 and 3.00 in red and the fibres with FPTI smaller than 2.00 in green. This colour combination helps to emphasise the differences between the FPTI indices of the compared mineral fibres. The FPTI threshold value that separates "safe" from "hazardous" fibres is assumed to be 2.00 (Gualtieri 2018). Fibres that have an FPTI value below this limit are considered as negative standards and are highlighted in green in the histogram. Instead, mineral fibres with FPTI > 2.00 are highlighted in red as potentially toxic and pathogenic. The black colour highlights the fibres with very high toxicity/pathogenicity potential.



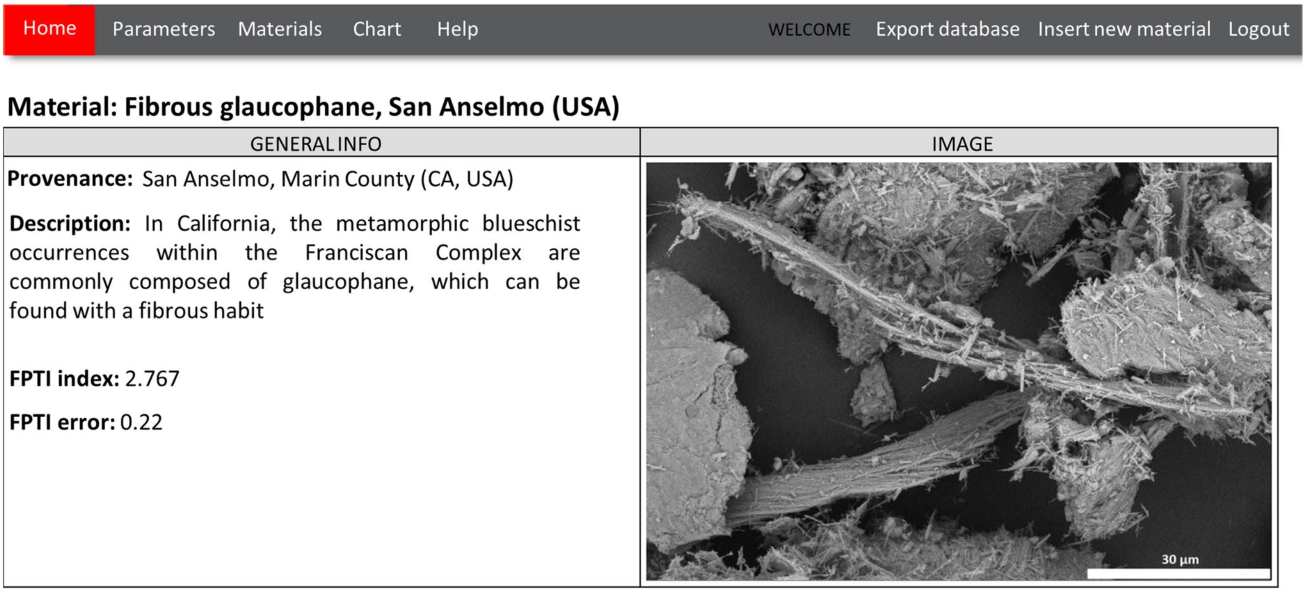
General information for the new material

Name of material:	Fibrous glaucophane	
Provenance:	San Anselmo, Marin	E.g. country, province, etc.
Description:	In California, the metamorphic blueschist occurrences within the Franciscan Complex	A short description (up to 512 characters) of the material
Upload a picture of the new material:	Select file	Upload .jpg or .png file

Parameter values for the new material

Parameter	Value	Suggestion	Error on value
Mean length:	4.0	Values range from less than 5.0 to over 20.0 (Micrometers)	0.0
Mean diameter:	0.22	Values range from less than 0.25 to over 3.0 (Micrometers)	0.02
Crystal curvature:	flat surface		Applied fixed error
Crystal habit:	acicular		Applied fixed error

Fig. 2 WebFPTI user interface. FPTI parameters and the associated error for fibrous glaucophane



Material: Fibrous glaucophane, San Anselmo (USA)

GENERAL INFO	IMAGE
Provenance: San Anselmo, Marin County (CA, USA) **Description:** In California, the metamorphic blueschist occurrences within the Franciscan Complex are commonly composed of glaucophane, which can be found with a fibrous habit **FPTI index:** 2.767 **FPTI error:** 0.22	

Fig. 3 WebFPTI user interface. Detailed report about fibrous glaucophane

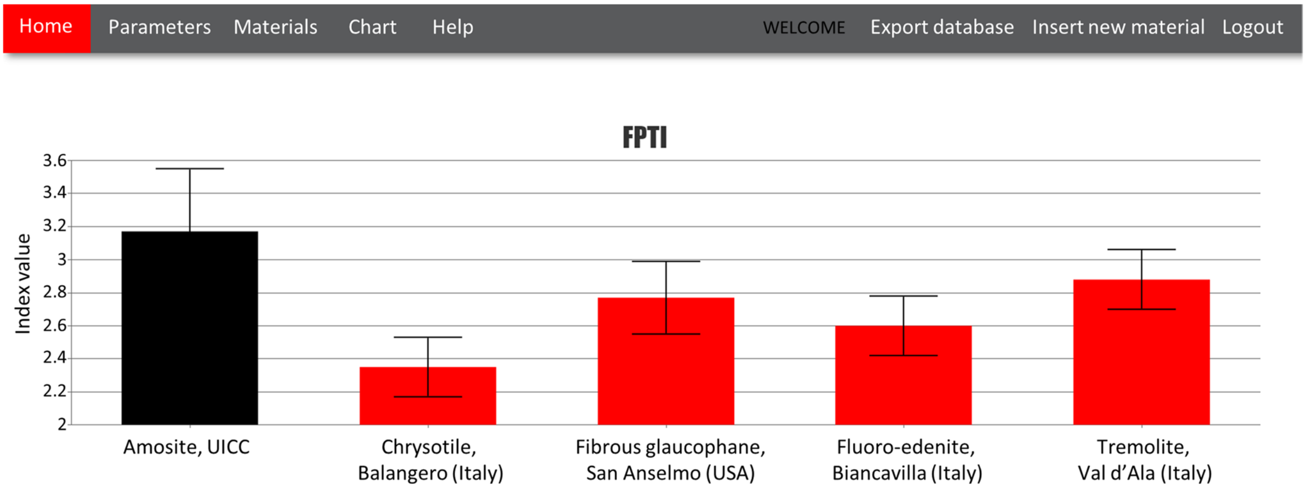


Fig. 4 WebFPTI user interface. FPTI calculated for fibrous glaucophane and other selected mineral fibres

Determination of FPTI of fibrous glaucophane

The software WebFPTI was recently used by the authors to calculate the FPTI of fibrous glaucophane from the metamorphic rocks outcropping in San Anselmo, Marin County, California (USA). Glaucophane is a sodic amphibole that may occur with a fibrous crystal habit in blueschist facies in former subduction zones like Franciscan Complex in California. Although crystalline habit and chemistry of fibrous glaucophane of Franciscan Complex make this mineral species analogous to asbestos, the effective health risks associated with its exposure has never been evaluated to date. In addition, as reported by Erskine and Bailey (2018), blueschist rocks from Franciscan Complex are commonly excavated for building/construction purpose in northern and central California and the dust generated by the excavation activities may potentially expose workers and the nearby populations to adverse health risks. Fibrous glaucophane from Franciscan Complex was fully characterized by Di Giuseppe et al. (2019) using a suite of experimental techniques. Data from Di Giuseppe et al. (2019) were used to fill in the fields required by the WebFPTI user interface to calculate the FPTI index (Fig. 2). Figure 4 shows a plot of the

FPTI index of fibrous glaucophane and other mineral fibre species, calculated by WebFPTI. The FPTI of fibrous glaucophane is markedly greater than that of chrysotile asbestos from the Balangero mine, and comparable to that of amphibole species like tremolite asbestos from Val d'Ala and fibrous fluoro-edenite from Biancavilla, both classified as carcinogens. The calculated FPTI of fibrous glaucophane indicates that this mineral fibre may represent a potential health hazard and, applying the precautionary approach, it should undergo a procedure of in vivo toxicity/pathogenicity testing. The prediction of the FPTI model that fibrous glaucophane from Franciscan Complex is a potential toxic/pathogenic mineral fibre is confirmed by the results of our recent in vitro toxicity study (Gualtieri et al. 2021). In particular, the results of in vitro tests show that fibrous glaucophane has the potential to induce cell death, DNA damage and oxidative stress.

Discussion

The occurrence in nature of unclassified mineral fibres is increasingly attracting the attention of authorities and organizations responsible for public and workers health. However, mineral fibre regulatory and legislative activities need the support of a consolidated methodology capable of recognizing and quantifying the health risk associated with these fibres. The aim of our study was to deliver WebFPTI, a tool aimed at assessing the potential toxicity/pathogenicity of all mineral fibre. The illustrative example reported in this work shows how easily the software manages a large amount of data (FPTI parameters) and readily provide the FTPI index value (Gualtieri 2018). Through a web interface, working in Software as a Service (SaaS) mode, WebFPTI allows the user to enter the parameters needed to calculate the FPTI index (Gualtieri 2018) and perform complex data processing that often not everyone can do. Moreover, the database of FPTI values allows the comparison of the toxicity/pathogenicity potential of different mineral fibres and especially asbestos minerals. Since WebFPTI is open source and accessible from all devices, it can serve as a tool for any user working with the environmental or health risk associated with unclassified mineral fibres. Thanks to WebFPTI it is eventually possible to quantify the environmental hazard related to the exposure to deposit, rocks and soil in which mineral fibres naturally occur and to protect workers who handle these natural materials. Therefore, WebFPTI can help authorities to identify the most efficient prevention programs, minimize costs and reduce any commercial, economic and public concerns.

Conclusions

WebFPTI is a predictive tool aimed at ranking the toxicity and pathogenicity potential of fibres like asbestos or unclassified mineral fibres. WebFPTI was designed so that an administrator or an external user can process the FPTI index parameters in a few minutes (although the experimental measurement of the parameters of the model, such as the dissolution rate, can take several months in the lab) and, at the same time, compare the results with the values obtained by the other users. The data collected are stored in a database and the administrator can allow the users (e.g. public authorities, heath organizations or researcher) to download data for external processing. This software can be used to improve mineral fibre classification methodologies (e.g., in vivo and in vitro tests) and thus to address the issues regarding the classification of the toxicity of unclassified mineral fibres compared to those regulated as asbestos. WebFPTI and the model behind it are live projects and in the future the community of users and researchers who will benefit and use our software will certainly help to develop and contribute to the projects. Meanwhile, in order to optimize the WebFPTI application, work is in progress to:

- Collect new experimental data to expand the WebFPTI database.
- Combine the current analytical predictive model with models based on machine learning approaches.
- Make the interface more user-friendly. For example, through the support of screencasts that show and train the use of the application tools.

Authors' contributions A.F.G. conceived the idea and wrote together with D.D.G. the manuscript with the contribution of all the co-authors. M.L. and L. R. made the web-based application. A.F.G, D.G.G. and A.Z. carried out the study concerning fibrous glaucophane.

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Data availability The user can access the WebFPTI application via the URL: http://fibers-fpti.unimore.it. The application can be accessed using a Web browser. To get "Contributing users" account, submit your request to one of these email addresses: mauro.leoncini@unimore.it, alessandro.gualtieri@unimore.it, dario.digiuseppe@unimore.it.

Declarations

Conflict of interest Authors confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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