Make the SMART move to PDF-4/Organics

A comprehensive diffraction database for phase identification combining both single crystal and powder diffraction data. All data sets are standardized, classified and edited for rapid, accurate, material identification.

International Centre for Diffraction Data

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Dear Customer,

We invite you to review the enclosed case studies that showcase the benefits of using a SMART database for your phase analyses. The PDF-4/Organics database is SMART. It is designed to solve difficult problems that are analyzed by powder diffraction analysis for a multitude of applications in the pharmaceutical, regulatory, specialty chemical, biomaterials and forensic fields. As you will discover in the following pages, the PDF-4/Organics database is both comprehensive with 479,278 entries, and highly targeted, with special focus on materials used in commercial and regulatory fields. We not only extract the public literature like other databases, we add unique content by extracting patent data, combining single crystal and powder references, combining organics with common inorganics and polymers, and continuously adding targeted materials through grants and research proposals. If we don't have what you need, we can get it!

The combination of single crystal and powder reference data provides the user with the ability to analyze both crystalline and noncrystalline solid state materials. This, in turn, allows the user to apply numerous pattern fitting techniques (Rietveld, LeBail, FullProf, FullPAT) to identify materials. This also allows the user to quantitate, measure crystallinity, and determine crystallite sizes.

Our goal is to help you solve your materials problems!

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PDF-4/Organics
The SMART Choice

SMART databases help you solve tough problems. You solve tough problems you get noticed. You get noticed and your value to your organization grows!

The PDF-4/Organics database is designed to solve difficult problems that are analyzed by powder diffraction analysis. It works seamlessly with commercial analysis software and integrated diffractometer systems and is compatible with dozens of software analysis programs including those of all major global powder diffraction equipment manufacturers. It can also be used as a stand-alone data analysis system to analyze conventional X-ray, synchrotron X-ray, or electron diffraction data.

If you work in law enforcement, forensic or pharmaceutical sciences your job is tough. It is always difficult to find the right tools for the right job. You are expected to analyze complex mixtures nondestructively, frequently with little sample, while following good lab practice protocols. To make matters worse, the materials that you are likely to analyze are often of low symmetry and have large unit cells (many peaks with lots of overlap). They crystallize in needles and platelets (orientation!) and are frequently in low concentration and diluted by fillers, pigments and other types of materials. In other words, your peak positions are often compromised. The intensities are crippled by orientation and you frequently are looking for a needle in a haystack! In addition, your material might not even be crystalline.

If this sounds like you, you need some help. You need a database that is intelligent and has had the input of experts that have been in your shoes, and is designed to help you at your job. You need a **SMART** database!

In these pages we hope to demonstrate what a **SMART** database does and how it can help you correctly identify and analyze materials for problems ranging from easy to most difficult.

HOW SMART IS YOUR DATABASE?

- **S**tandardized data
- **M**ore coverage
- **A**ll data sets are evaluated for quality
- **R**eviewed, edited and corrected prior to publication
- **T**argeted for material identification and characterization

Having a **SMART** database means that your database is not just a collection of numbers, but is organized in such a way as to improve your ability to analyze materials and solve problems. This means that the content is targeted and the data are standardized and organized to facilitate identification and quantitative analyses.

Having a **SMART** database means that it doesn't matter whether you use a 1 or 2 dimensional detector or that you use conventional X-rays, synchrotron X-rays, or electrons. The database can handle it.

Having a **SMART** database means you can match high quality data to high quality references resulting in identification of more materials at lower concentrations. You not only get the most out of your database, but the most out of your equipment. ICDD is the only database organization that tells you about the quality of every reference. We are also the only crystallographic database organization that is ISO 9001:2008 certified.

Having a **SMART** database means that 130 fields are displayed, 57 can be searched, and 92 can be sorted and graphed allowing the user to create appropriate subsets of the database and get the correct answers to the most difficult problems. It means that you can data mine millions of pieces of information in nearly endless combinations.

BE SMART - Get the correct answer!

PDF-4/Organics, the **SMART** database, uses subfiles to identify materials of the appropriate chemistry. This is a unique feature of the database and it greatly enhances the user's ability to identify the correct phase by eliminating false positives. The classification of materials into subfiles is performed by ICDD editors in collaboration with field experts; many of whom are volunteer member scientists of the ICDD. This includes chemists, mineralogists, pharmaceutical scientists, and forensic scientists. This is a manually intensive effort that has been conducted for most of ICDD's >70 year history. When you purchase PDF-4/Organics, you receive the benefits of the collective knowledge of experts.

Any large database will contain millions of reference d-spacings and any experimental pattern of sufficient complexity will match phases in a large database, even if your specimen components aren't contained in the database (i.e., trying to identify drugs in a database of metals). With today's automated software you will get a "match" even when the chemistry is inappropriate. The PDF-4/Organics is an extremely large database having over 91 million d-spacings contained in its 479,278 references. As a **SMART** database, we help the user identify the correct materials by providing filters so that they search on the correct subfiles. The database also contains a large collection of additional filters so that the user can search on composition, chemical nomenclature, structural classes, prototype structures or physical properties.

The database contains several statistical analysis tools enabling you to evaluate the quality of the references and the quality of your match and identification. These provide you with the confidence that you have the correct solution for your analysis.

Software Capabilities

- *All data expressed as digital patterns*
- *Crystallite size function*
- *Preferred orientation function*
- *Data import, background correction, smoothing, peak finding*
- *Search and identification using 4 different algorithms*
- *Molecular displays and interactive graphics*
- *Spot pattern, ring pattern, EBSD pattern simulations*

GET THE BEST OF BOTH WORLDS - SINGLE CRYSTAL AND POWDER DIFFRACTION DATA

PDF-4/Organics contains powder diffraction data collected from the world literature (including patents), donations by various worldwide institutions, and data collected for more than 50 years through the ICDD's Grant-in-Aid program. The ICDD has also received data from collaborations with single crystal database organizations. This includes organic and organometallic materials from the Cambridge Crystallographic Database and inorganic excipients from the ICSD and NIST data collections.

Single crystal data and experimental powder data can be very complimentary in powder diffraction analyses. Experimental powder patterns are very useful for materials that are difficult to crystallize, are nanocrystalline, or are amorphous. Many noncrystalline materials have reproducible chemistries and X-ray scattering patterns that can be used as references. This includes most polymers and many active pharmaceutical ingredients. Furthermore, the vast majority of powder diffraction reference data were collected at room

	Powder Sourced Data	Single Crystal Sourced Data	Entries with Atomic Coordinates
Forensics	**2,342**	**1,991**	**1,671**
Pharmaceuticals	**3,938**	**4,353**	**4,177**
Excipients	**588**	**1,434**	**1,336**
Polymers	**1,192**	**221**	**180**
Pigments	**521**	**284**	**297**

Table 1. Multiple sources provide extensive coverage of critical materials for many of the subfiles.

temperature helping any user that is trying to identify an unknown material at room temperature (i.e., nearly all law enforcement laboratories). This is one of the reasons why powder diffraction references are often preferred over nonambient single crystal references in search/match processes.

Single crystal data are useful in confirming chemical composition, providing structural information and atomic coordinate sets useful in quantitative analysis by Rietveld refinements. In Table 1, one can see that PDF-4/Organics contains a high percentage of the available atomic coordinate sets in targeted subfiles.

A historic collaboration between ICDD and the Cambridge Crystallographic Database provided organic and organometallic content to PDF-4/Organics for all publications up through the publication year 2010. However, atomic coordinates, useful for Rietveld analyses, were not included with this agreement. Since 2010, ICDD bibliographers and editors have been adding atomic coordinate sets for both newly published materials and historic literature, specifically targeted at commercial materials, as shown in Table 1. The ICDD editors are also adding important information, such as site occupancy factors and anisotropic thermal displacement parameters.

Getting the right materials in the right subfiles also means that ICDD specifically searches not only publications, but patents and trade names. The latter two are heavily associated with commercial materials, which can be identified and classified.

BETTER QUANTITATIVE RESULTS

Over the last decade, there have been numerous methods devised for quantitative phase analysis by diffraction methods. Most of the methods are based on total pattern analysis, some are fitting methods, others, such as Rietveld, fit and refine. PDF-4/Organics includes digital patterns, I/Ic, atomic coordinates, and indexed unit cells to enable a very wide range of quantitative analysis techniques. PDF-4/Organics includes embedded software for scaling and adding patterns, as well as an "intelligent" RIR calculation for semi-quantitative analysis. Also included is a similarity index program that can be used to identify materials, even noncrystalline materials. You can also use commonly available Rietveld software to fit and refine structures. All PDF-4/Organics entries can be exported in CIF format for use with dozens of programs. The PDF-4/Organics database also contains integrated molecular display programs (as shown in Figure 1), bond angle and distance calculators and nearest atom displays, which are useful for interpreting pair distribution function data.

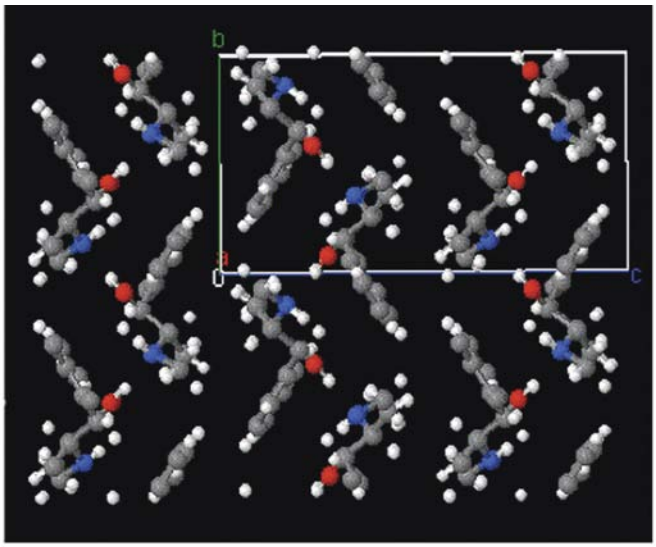

Figure 1. The molecular packing diagram for (+)-pseudoephrine as viewed down the a-axis.

ENHANCED IDENTIFICATION - CRYSTALLINE, NANOCRYSTALLINE AND AMORPHOUS MATERIALS

In the materials world, there are many solids that are not crystalline. There are also many nanomaterials that have ordered cores and various types of surface defects. If the materials are reproducible and have characteristic powder patterns, they can be identified. Your identification can include polymers, clays, amorphous active pharmaceutical ingredients, API's, and a wide range of nanomaterials. When it comes to materials, our database has guidelines, not rules. We include all materials that help you do an analysis. In addition to the excipients mentioned previously, PDF-4/Organics includes common inorganic salts and corrosion products. It's a **SMART** database designed to solve problems.

SOME SPECIFIC DEVELOPMENTS

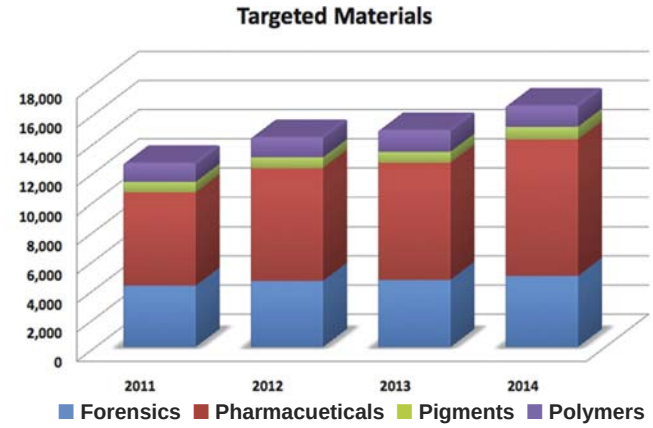

Figure 2.

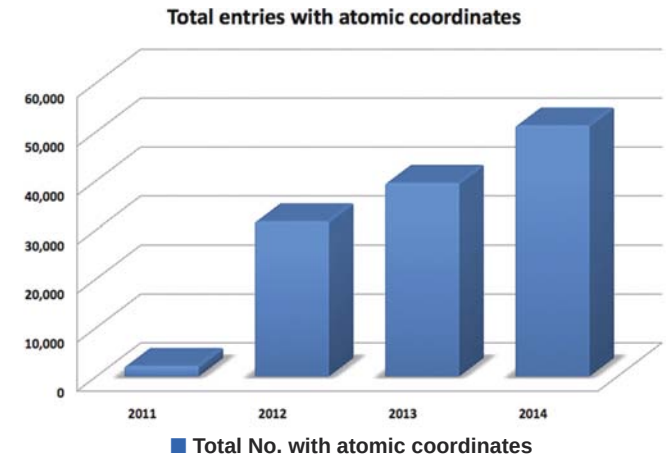

Figure 3.

As shown above, Figures 2 and 3, we continue to add targeted materials and atomic coordinates annually. Our efforts are focused on the targeted materials, contained in "expert" subfiles developed by our field experts and enhanced by our editors.

We also continue to solicit data via the ICDD Grant-in-Aid program to add new materials to the database. This program supports researchers' work on characterization of natural products, pigments, polymers and pharmaceuticals.

An extensive study, performed in 2012-13, identified many commercial drugs that have not been characterized by either powder diffraction or single crystal diffraction studies. The ICDD, in collaboration with Argonne National Laboratory and Illinois Institute of Technology, is currently obtaining these materials, having reference patterns collected, and performing structure solution through powder methods. This is expected to be a multi-year effort. The first data have already been collected and several structures solved. They are being processed for future editions of the database. Much of this data will be first published in our journal, *Powder Diffraction*.

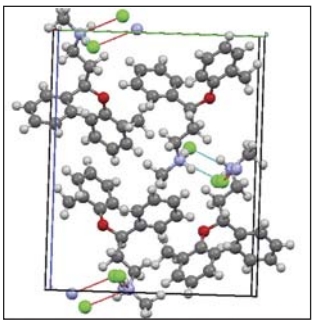

Figure 4. Unit cell and molecular structure for atomoxetine hydrochloride. The structure was solved and refined using synchrotron powder diffraction data, and Rietveld and density functional techniques.

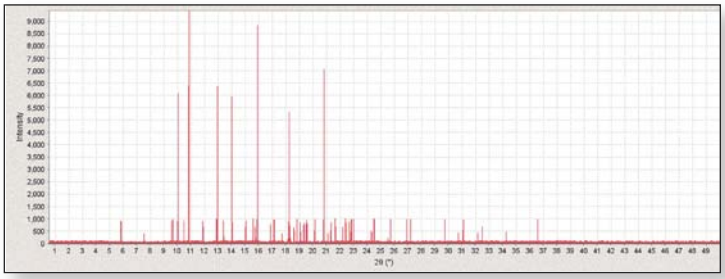

Figure 5. The powder diffraction pattern of atomoxetine hydrochloride produced through an ICDD Grant-in-Aid with collaborative agreement with X-ray Operations Research Division, Advance Photon Source, Argonne National Laboratory, to be published in Powder Diffraction.

CONTINUOUS DEVELOPMENT

PDF-4/Organics undergoes continuous annual development as we continue to extract and evaluate new data from the literature and commission new data from grants. We also add new software capabilities to the database in response to user requests. Collaborations with field experts and constant feedback from our members and customers ensure that we continue to add features that are useful to the scientific community.

EDUCATION

Our goal is to help you solve your material problems.

In addition to the PDF-4/Organics database, we also provide online publications and tutorials. Many tutorials focus on capabiltities of the database, but there are also general tutorials that describe methods used to analyze drugs, polymorphic composition and polymers. There are links to free download publications on pharmaceutical analysis, but also over 931 full publications for free download from Advances in X-ray Analysis. Our website, tutorial page and publication page are there to help you!

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CASE STUDY: FORMULATION ANALYSIS OF LIPITOR®

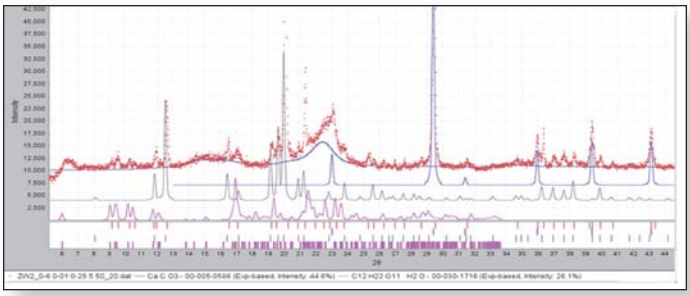

Figure 1. The diffraction pattern (red) from a crushed tablet of Lipitor®. The digital patterns underneath are the digital patterns of the ingredients identified from the PDF-4/Organics database.

Diffraction analyses of Lipitor® identify the major ingredients as calcium carbonate, microcrystalline cellulose, lactose monohydrate, and the active pharmaceutical ingredient (API) calcium atorvastatin. In developing a database that could analyze complex formulation problems, the scientist members of ICDD quickly found out that they needed a collection of pharmaceutical excipients to identify the inert components. The excipients could be inorganic materials, such as calcium carbonate or polymeric materials, such as microcrystalline cellulose. In 2002, an Excipient subfile was created and populated for the PDF-4/Organics database, which included all classified excipients. The excipient additions since that time added thousands of inorganic and polymeric materials to the database. This is because the design of the database is to help users solve problems, not to adhere to chemical rules.

During development of the database and product testing it also became apparent that many pharmaceutical components were nanocrystalline, semicrystalline or amorphous. The database now includes a diffraction pattern simulator for nanomaterials (added in 2005), as well as microcrystalline and amorphous full-pattern references. In the case of Lipitor®, this allows the user to identify the nanocrystalline phase of cellulose Iβ, in the structural identification of microcrystalline cellulose.

Most reference patterns of active pharmaceuticals in the database arise from either powder diffraction reference data or single crystal calculated patterns. The active ingredient in Lipitor® was identified through references from the patent literature. Calcium atorvastatin has many polymorphic forms, therefore many references. The specific API identified was calcium atorvastatin trihydrate.

Finally, the pattern for Lipitor® can be compared to a summed pattern of the ingredients. However, the match was not perfect. This is because the lactose monohydrate has a platelet morphology and exhibits an oriented diffraction pattern. The final step in this analysis was to model the preferred orientation (along (100)) using a orientation function built into the PDF-4/Organics database. The final agreement is shown in Figure 2.

PDF-4/Organics, the **SMART** database, includes preferred orientation functions, crystallite size simulators, pattern display and summation, an Excipient subfile and nanocrystalline references, all of which were used to solve this problem. The API was identified through ICDD references generated from the patent literature.

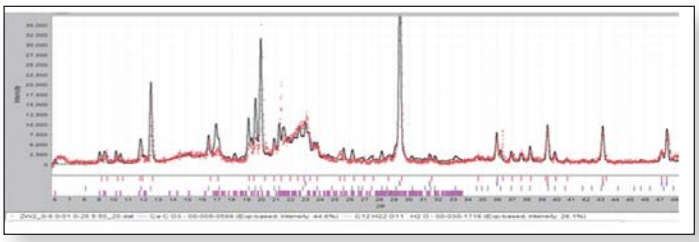

Figure 2. The diffraction pattern (red) from a crushed tablet of Lipitor® as compared to a composite pattern from the four identified ingredients (black).

The figures and analyses provided with this case study were entirely performed with the embedded software contained in PDF-4/Organics. This problem could not be solved by any other database in the world.

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CASE STUDY: CENTRUM PERFORMANCE®

Figure 1. The diffraction pattern (red) from a crushed tablet of Centrum Performance®.

The diffraction analysis of Centrum Performance® presents several challenges due to the large number of ingredients used in the formulation and the extreme range of their concentrations. This means that there are hundreds of peaks, which need to be accounted for in the pattern.

The data set shown in Figure 1 was collected at the Argonne Advanced Photon Source synchrotron. The high intensity of the synchrotron beam resulted in 234 peaks being identified in the pattern with a range of intensities covering four orders of magnitude (Imax having over 400,000 counts).

Common Name	Formula
Calcite	$CaCO_3$
Monetite	$CaHPO_4$
Brushite	$CaHPO_4 \cdot 2H_2O$
Vitamin C	$C_6H_8O_6$
Sylvite	KCl
Zincite	ZnO
Periclase	MgO
Fe Fumarate	$Fe(C_2H_2O_4)$
Nicotinamide	$C_6H_6N_2O$
Cellulose Iβ	$(C_6H_{10}O_5)_n$

Table 1.

Table 1. The ingredients identified by the diffraction analysis using the integrated program Sleve+ in PDF-4/Organics. Overall, ten ingredients were positively identified and 212 out of the 234 peaks were assigned to these 10 phases. The references used in the identification came from a combination of powder diffraction and single crystal reference sources. All the references used in the identification were either high quality (S or I) or resulting from Rietveld refinement. The identification process used the Pharmaceutical and Excipients subfile in the PDF-4/Organics to search only on ingredients that are known to be in pharmaceutical formulations. We obtained similar results using a high quality laboratory diffractometer equipped with an incident beam monochromator (Kα1).

PDF-4/Organics, the **SMART** database, is able to analyze synchrotron data from general user facilities just as easily as you analyze data from your laboratory diffractometer. The simulation software in the database includes instrument functions for synchrotron data and the ability to input any monochromatic wavelength typical of synchrotron operations. PDF-4/Organics enables the user to match the highest quality data from either lab instruments, or synchrotrons, with high quality references due to the comprehensive number of references, many of which are high quality. The ten phase identification with hundreds of matched peaks demonstrates that even the most complex samples can be properly analyzed.

The figures and analyses provided with this case study were entirely performed with the embedded software contained in PDF-4/Organics. This problem could not be solved by any other database in the world.

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CASE STUDY: NANOMATERIALS

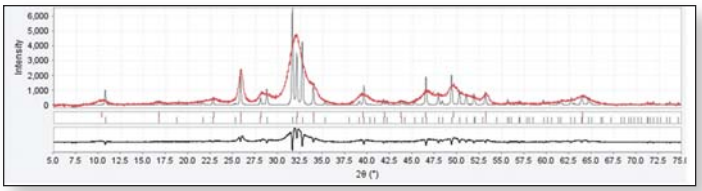

Figure 1. The diffraction pattern of nanocrystalline hydroxyapatite that was produced by Transparent Materials LLC. The experimental pattern (red) is being developed as a reference material and is compared to a reference pattern of a highly crystalline hydroxyapatite (grey) with a difference pattern calculated in black.

This material would be difficult to identify using standard search/match procedures because the nanocrystalline line broadening merges several characteristic d-spacings into single peaks that are shifted from the expected positions due to peak overlap. Embedded software in PDF-4/Organics can be used to identify the material (via Similarity Index), characterize the crystallite size (90 Å), and measure the orientation of the crystallites (along (100)). The agreement between the experimental and modeled pattern is shown below.

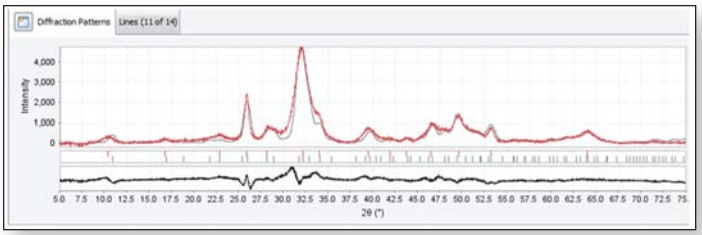

Figure 2. Experimental data (red) compared to a simulated hydroxyapatite of 90 Å crystallite size and oriented along [100] (grey).

Electron microscopy confirms both the size and platelet morphology (orientation) of the specimen. In an actual application, we have used the nanomaterial reference to identify nanohydroxyapatite in a commercial fertilizer.

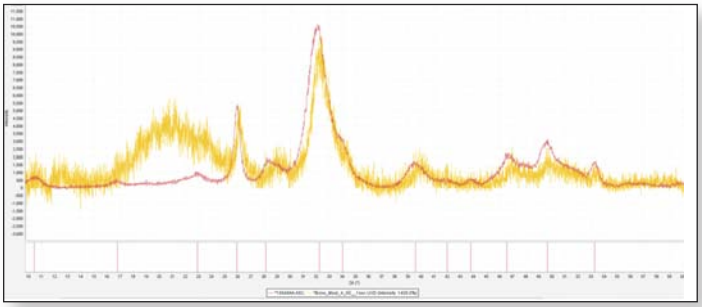

Figure 3. Identification of nano-apatite in commericial bone fertilizer.

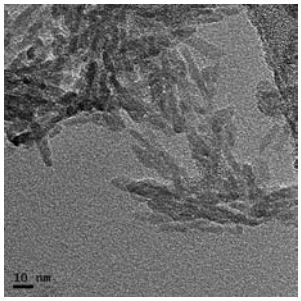

Figure 4. Photo of nano-apatite. Photo and specimen courtesy of Transparent Materials, LLC.

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