綠色/永續化學資訊共享 2013.07.01

彰化師範大學化學系 林秋薰教授

As green chemistry emphasizes that chemists should have an understanding of the principle of Toxicology of the chemicals that we are using. A few papers on the potential toxicity when applying nanomaterials are added. Thus, the contents for this issue of Green Chemistry Communication are divided as the followings: (I) Green chemistry meetings (items 1-11, pp. 1-2), (II) On-line seminar: CO_2 utilization (items 12-16, pp. 2-4), (III) Interesting developments in green chemistry (items 17-30, pp.4-12), and (IV) Toxicity arising from applying nanomaterials and nanotechnology(items 31-41, pp.12- 22).

I. **Green Chemistry Meetings**: Through December, 2013

(1) ACS Summer School on Green Chemistry and Sustainable Energy, July 22 – July 29, 2013, Golden, Colorado.

(2) 6th International Conference on Green and Sustainable Chemistry, August 4-7, 2013, Nottingham, United Kingdom.

(3) ICOSSE '13 - 3rd International Congress on Sustainability Science & Engineering, August 11-15, 2013, Cincinnati, Ohio, USA.

(4) 246th ACS National Meeting & Exposition, September 8-12, 2013, Indianapolis, Indiana, USA

(5) Sustainable Chemistry 2013, September 3-5, 2013, New Forest, United Kingdom.

(6) 1st EuCheMS Congress on Green and Sustainable Chemistry, October 13-15, 2013, Budapest, Hungary.

(7) 10th Green Chemistry Conference, November 5-7, 2013,Barcelona, Spain.

(8) Ecochem, November 19-21, 2013, Basel, Switzerland.

(9) 3rd Industrial Green Chemistry World (IGCW), December 4-6, 2013
Mumbai, India

(10) Gordon Research Seminar, July 26-27, 2014, The Chinese University of Hong Kong, Hong Kong, China.

(11) 4th Asia-Oceania Conference on Green and Sustainable Chemistry (AOC-4 GSC), November 2-6, 2013, New Taipei City Hall, Taiwan.
Website: http://aoc-4.web.nthu.edu.tw

II. On-line Seminar: an old but interesting speech on June 6, 2013.

(12) ACS Webinars – Innivations in green chemistry: organics from carbon dioxide, sunlight and water

What You Will Learn

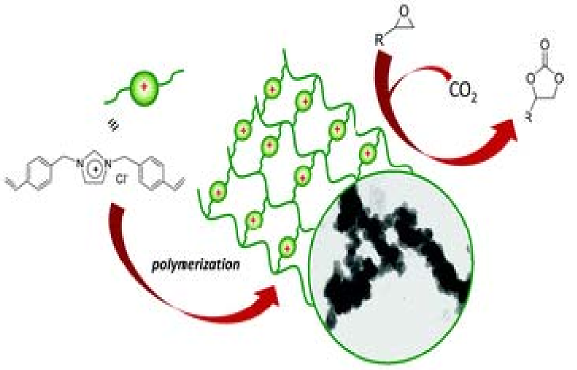
- The energy cost of using CO_2 as a starting material for fuels and/or organic products.
- Novel electrocatalysts that promote the efficient conversion of aqueous CO_2 to alcohols.
- How can we drive CO_2 to organics using sunlight: The search for solar fuels?
- Is CO_2 chemistry the fun and games of university profs, or is there a sound, near term, business challenge that can take advantage of this chemistry?

Read also the followings:

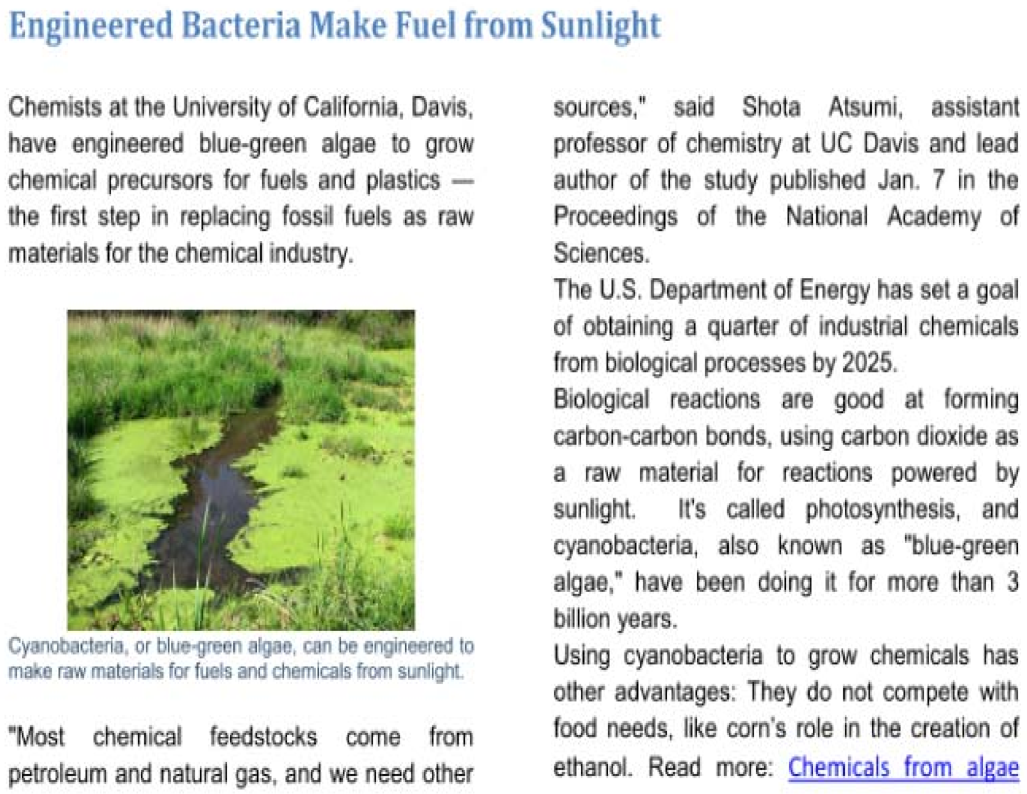
(13) Frontiers, opportunities, and challenges in biochemical and chemical catalysis of CO_2 fixation, Chem. Rev., Articles ASAP. DOI: 10.1021/cr300463y

(14) Cycloaddition of CO_2 to epoxides catalyzed by imidazolium-based polymeric ionic liquids: ***Green Chem.***, 2013,**15**, 1584-1589. **DOI:** 10.1039/C3GC37085B

A series of cross-linked ionic polymers based on styrene-functionalized imidazolium salts with chloride, hexafluorophosphate, or tetrafluoroborate counter anions have been prepared and characterized using a range of analytical and spectroscopic techniques and electron microscopy. The polymer with the chloride anion is an efficient catalyst for the cycloaddition of carbon dioxide with epoxides to afford cyclic carbonates. The cross-linked polymer is insoluble in organic solvents and is highly stable and therefore can be easily recycled and reused.



(15) Biological fixation of CO_2:



Engineered Bacteria Make Fuel from Sunlight

Chemists at the University of California, Davis, have engineered blue-green algae to grow chemical precursors for fuels and plastics — the first step in replacing fossil fuels as raw materials for the chemical industry.

Cyanobacteria, or blue-green algae, can be engineered to make raw materials for fuels and chemicals from sunlight.

"Most chemical feedstocks come from petroleum and natural gas, and we need other sources," said Shota Atsumi, assistant professor of chemistry at UC Davis and lead author of the study published Jan. 7 in the Proceedings of the National Academy of Sciences.

The U.S. Department of Energy has set a goal of obtaining a quarter of industrial chemicals from biological processes by 2025.

Biological reactions are good at forming carbon-carbon bonds, using carbon dioxide as a raw material for reactions powered by sunlight. It's called photosynthesis, and cyanobacteria, also known as "blue-green algae," have been doing it for more than 3 billion years.

Using cyanobacteria to grow chemicals has other advantages: They do not compete with food needs, like corn's role in the creation of ethanol. Read more: Chemicals from algae

(16) New CO_2 Journal:

Journal of CO_2 Utilization

The Journal of CO2 Utilization offers a single, multi-disciplinary, scholarly platform for the exchange of novel research in the field of CO_2 re-use for scientists and engineers in chemicals, fuels and materials.

The emphasis will be on the dissemination of leading-edge research from basic science to the development of new processes, technologies and applications. This includes CO_2 as a feedstock in the chemical, energy and materials sectors, and utilization in general to help minimize environmental impact.

The ***Journal of CO_2 Utilization*** will publish **original peer-reviewed research papers, reviews, and short communications**, including experimental and theoretical work, and analytical models and simulations.

The coverage includes, but is not limited to:

- Materials for CO_2 activation and adsorption
- Heterogeneous and homogeneous catalytic reactions involving CO_2
- CO_2 conversion to generate synthetic fuels, polymers, organic carbonates, and intermediate products.
- Supercritical CO_2 utilization in natural product extraction, catalysis and separation
- Use of CO_2 as an oxidant
- Electrochemical conversion of CO_2
- Photo-electrochemical, photo-catalytic and photochemical conversion of CO_2
- Biological conversion of CO_2
- Chemical looping combustion processes and technologies for CO_2 reduction

III. Interesting Developments in Green Chemistry:

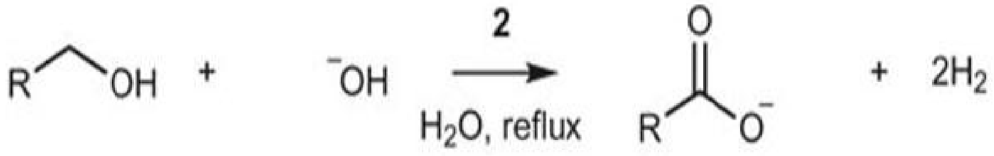
(17) Benign by design: catalyst-free in water, on water green chemical methodologies in organic synthesis: **Chem. Soc. Rev.**, 2013, **42**, 5522. DOI: 10.1039/c3cs60025d

Catalyst-free reactions developed during the last decade and the latest developments in this emerging field are summarized with a focus on catalyst-free reactions in-water and on-water. Various named reactions, multi-component reactions and the synthesis of heterocyclic compounds are discussed including the use of various energy input systems such as microwave- and ultrasound irradiation, among others. Organic chemists and the practitioners of this art both in academia and industry hopefully will continue to design benign methodologies for organic synthesis in aqueous media under catalyst-free conditions by using alternative energy inputs based on fundamental principles.

Fig. 1 The ideal synthesis.

(18) Catalytic transformation of alcohols to carboxylic acid salts and H_2 using water as the oxygen atom source: **Nature Chemistry**, **5**,122, 2013. doi:10.1038/nchem.1536

The oxidation of alcohols to carboxylic acids is an important industrial reaction used in the synthesis of bulk and fine chemicals. Most current processes are performed by making use of either stoichiometric amounts of toxic oxidizing agents or the use of pressurized dioxygen. Here, we describe an alternative dehydrogenative pathway effected by water and base with the concomitant generation of hydrogen gas. A homogeneous ruthenium complex catalyses the transformation of primary alcohols to carboxylic acid salts at low catalyst loadings (0.2 mol%) in basic aqueous solution. A consequence of this finding could be a safer and cleaner process for the synthesis of carboxylic acids and their derivatives at both laboratory and industrial scales.

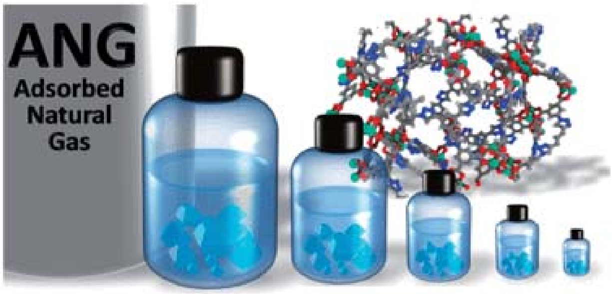


(19) Metal–organic frameworks as platforms for clean energy: ***Energy Environ. Sci.***, 2013,**6**, 1656. **DOI:** 10.1039/C3EE40507A

In order to void environmental pollution and an energy shortage, the application of clean and renewable energy, such as solar, instead of fossil fuel is foreseen as a prospective issue. It is urgent and important to develop and optimize various energy storage and conversion technologies and materials aimed at utilization of different clean energy sources. Metal–organic frameworks (MOFs), a new class of porous crystalline materials, act as an outstanding candidate in this field based on their high surface areas, controllable structures and excellent electrochemical properties. Here, selected recent and significant advances in the development of MOFs for clean energy applications are reviewed, and special emphases are shown to the applications of MOFs as platforms for hydrogen production and storage, fuel cells, Li-ion rechargeable batteries, supercapacitors and solar cells.

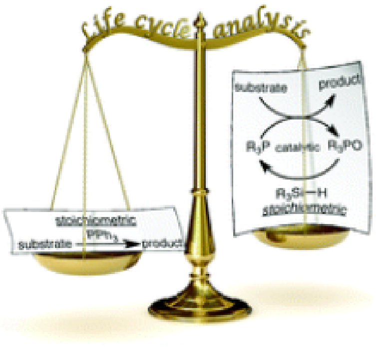
(20) <u>Gram-scale, high-yield synthesis of a robust metal–organic framework for storing methane and other gases:</u> ***Energy Environ. Sci.***, 2013,**6**, 1158. **DOI:** 10.1039/C3EE24506C

We have synthesized and characterized a new metal–organic framework (MOF) material, **NU-125**, that, in the single-crystal limit, achieves a methane storage density at 58 bar (840 psi) and 298 K corresponding to 86% of that obtained with compressed natural gas tanks (CNG) used in vehicles today, when the latter are pressurized to 248 bar (3600 psi). More importantly, the deliverable capacity (58 bar to 5.8 bar) for **NU-125** is 67% of the deliverable capacity of a CNG tank that starts at 248 bar. (For crystalline granules or powders, particle packing inefficiencies will yield densities and deliverable capacities lower than 86% and 67% of high-pressure CNG.) This material was synthesized in high yield on a gram-scale in a single-batch synthesis. Methane adsorption isotherms were measured over a wide pressure range (0.1–58 bar) and repeated over twelve cycles on the same sample, which showed no detectable degradation. Adsorption of CO_2 and H_2 over a broad range of pressures and temperatures are also reported and agree with our computational findings.



(21) <u>On the usefulness of life cycle assessment in early chemical methodology development: the case of organophosphorus-catalyzed Appel and Wittig reactions:</u> ***Green Chem.***, 2013,**15**, 1255. **DOI:** 10.1039/C3GC00053B

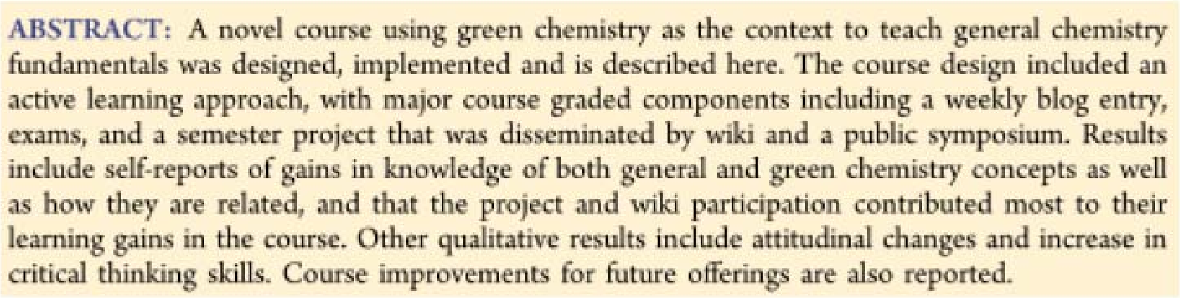
Recently, catalytic methodologies have been developed to avoid phosphine oxide waste produced in classic phosphorus-consuming processes, *i.e.* Appel and Wittig reactions. For these new catalytic methods, however, the requisite stoichiometric amounts of silanes raised the question of whether net environmental improvements can be achieved. Here, we conducted a life cycle assessment (LCA), in which the classic reactions are compared with their catalytic counterparts in terms of cumulative energy demand and greenhouse gas emissions. The analysis shows that the replacement of phosphines by silanes can offer environmental improvements for the Wittig reaction, but that additional reagents and working in lower concentrations can offset these environmental improvements for the Appel reaction. These results clearly show the importance of LCA in early chemical methodology development.

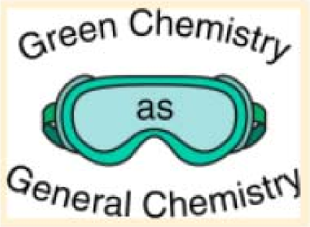


(22) Barriers to the Implementation of Green Chemistry in the United States: **Environ. Sci. Technol.**, 2012, **46** , 10892. **DOI:** 10.1021/es3021777

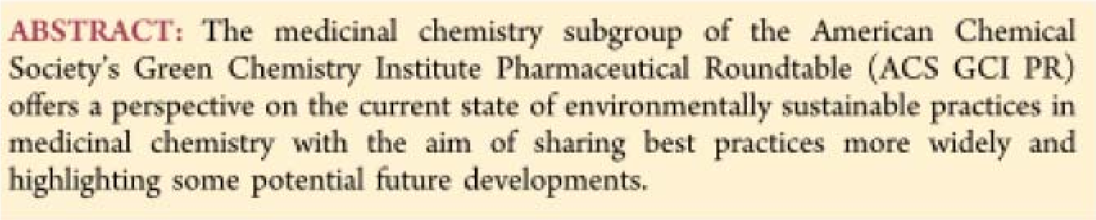
This paper investigates the conditions under which firms are able to develop and implement innovations with sustainable development benefits. In particular, we examine “green chemistry” innovations in the United States. Via interviews with green chemistry leaders from industry, academia, nongovernmental institutions (NGOs), and government, we identified six major categories of challenges commonly confronted by innovators: (1) economic and financial, (2) regulatory, (3) technical, (4) organizational, (5) cultural, and (6) definition and metrics. Further analysis of these barriers shows that in the United States, two elements of these that are particular to the implementation of green chemistry innovations are the absence of clear definitions and metrics for use by researchers and decision makers, as well as the interdisciplinary demands of these innovations on researchers and management. Finally, we conclude with some of the strategies that have been successful thus far in overcoming these barriers, and the types of policies which could have positive impacts moving forward.

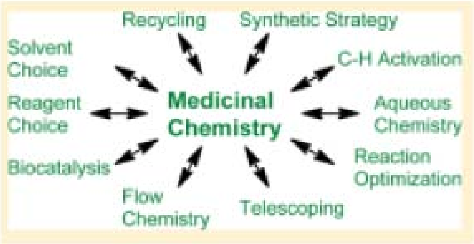
(23) Green Goggles: Designing and Teaching a General Chemistry Course to Nonmajors Using a Green Chemistry Approach: **J. Chem. Educ.**, 2013, **90**, 423. **DOI:** 10.1021/ed300538d


ABSTRACT: A novel course using green chemistry as the context to teach general chemistry fundamentals was designed, implemented and is described here. The course design included an active learning approach, with major course graded components including a weekly blog entry, exams, and a semester project that was disseminated by wiki and a public symposium. Results include self-reports of gains in knowledge of both general and green chemistry concepts as well as how they are related, and that the project and wiki participation contributed most to their learning gains in the course. Other qualitative results include attitudinal changes and increase in critical thinking skills. Course improvements for future offerings are also reported.



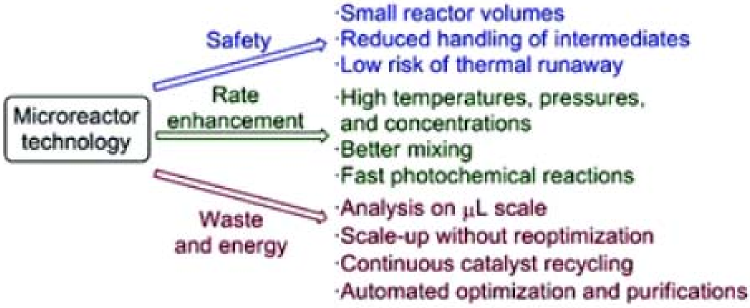
(24) Sustainable Practices in Medicinal Chemistry: Current State and Future Directions: **Journal of Medicinal Chemistry**, Just Accepted. **DOI:** 10.1021/jm400250p


ABSTRACT: The medicinal chemistry subgroup of the American Chemical Society's Green Chemistry Institute Pharmaceutical Roundtable (ACS GCI PR) offers a perspective on the current state of environmentally sustainable practices in medicinal chemistry with the aim of sharing best practices more widely and highlighting some potential future developments.



(25) The role of flow in green chemistry and engineering: **Green Chem.**, 2013,**15**, 1456. DOI: 10.1039/C3GC40374B

Flow chemistry and continuous processing can offer many ways to make synthesis a more sustainable practice. These technologies help bridge the large gap between academic and industrial settings by often providing a more reproducible, scalable, safe and efficient option for performing chemical reactions. In this review, we use selected examples to demonstrate how continuous methods of synthesis can be greener than batch synthesis on a small and a large scale.



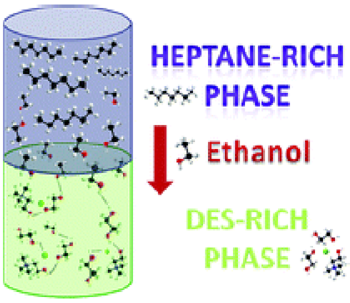
(26) Nontoxic solvents extract compound from plants (natural deep eutectic solvents): **C&E News**, June 6, 2013. **（此則信息由中研院化學所趙奕姼教授提供）**
http://cen.acs.org/articles/91/web/2013/06/Nontoxic-Solvents-

Natural Products: Green solvents made from mixtures of cellular metabolites coax pigments from safflowers

Read also the following article in the news: Are Natural Deep Eutectic Solvents the Missing Link in Understanding Cellular Metabolism and Physiology? Plant Physiology, 2011, **156**, 1701. DOI: 10.1104/pp.111.178426

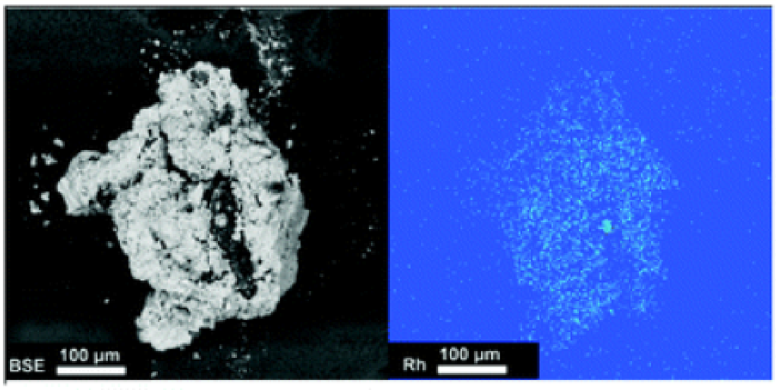
(27) Deep eutectic solvents as extraction media for azeotropic mixtures: ***Green Chem.***, 2013,**15**, 1326. **DOI:** 10.1039/C3GC37030E

The separation of azeotropic mixtures is an "old" engineering problem that cannot be solved by simple distillation processes. One of the current ways to overcome this problem is to use other types of processes, such as extractive/azeotropic distillation or liquid–liquid extraction, where entrainers or extraction solvents are applied. Liquid–liquid extraction processes have been emerging as appealing alternatives because they do not require high amounts of energy, volatile organic compounds or high pressures. In this work, deep eutectic solvents (DES) are tested as extraction solvents in the liquid–liquid separation of azeotropic mixtures. For this study three different DES, all based on choline chloride, were used for the liquid–liquid separation of an azeotropic mixture of heptane + ethanol at 25 °C. The feasibility of DES as extraction solvents was assessed by the determination of their selectivities and distribution coefficients, and compared with the literature. The data obtained show that DES surpass the performance of existing extraction solvents, leading to an increase in efficiency and a reduction in energy consumption of the overall process.

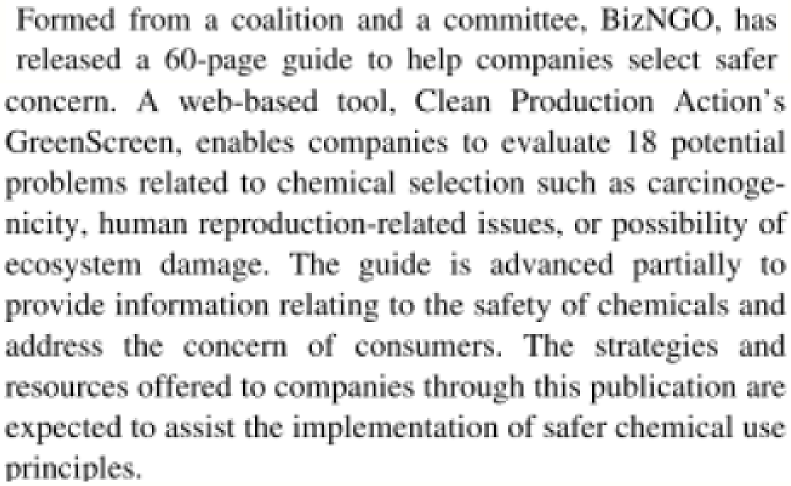


(28) Sustainable catalysts for methanol carbonylation: ***Green Chem.***, 2013,**15**, 1600. **DOI:** 10.1039/C3GC00024A

Methanol carbonylation is the most important process for manufacturing C2 molecules from methanol. The present industrial carbonylation has been proven to be the most successful process on economical grounds. However, there is a request to develop more sustainable and 'green' processes to overcome the inherent drawbacks. Well-designed cross-linked copolymers were prepared and used as support for the simultaneous immobilization of rhodium and iodide species. The resulting catalyst was proven to be highly active in CH_3I-free methanol carbonylation and methyl acetate was the main product. Approximately 90% of methanol was converted after a two-hour reaction time at 120 °C under a CO pressure of 3.0 MPa. The immobilization strategy of the active species works efficiently and the present methanol carbonylation catalyst shows good recyclability. After regenerating the catalyst twice over a fifteen-batches test, the catalyst keeps an acceptable activity. The process based on the present catalyst is evidently a promising sustainable methanol carbonylation



(29)Safer chemical guide: http://www.bizngo.org/giude.php. **(此則信息由台大化學系劉廣定教授提供)**

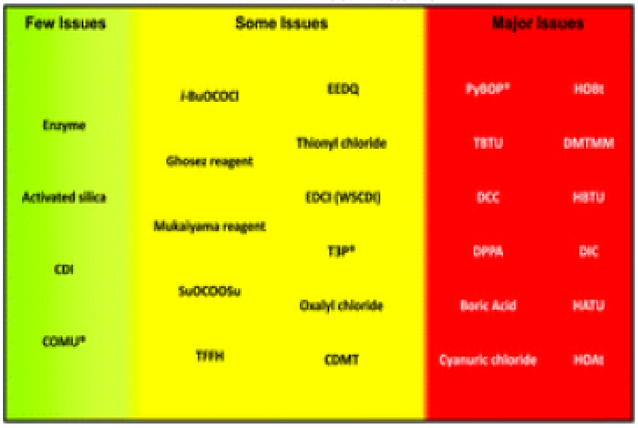


Formed from a coalition and a committee, BizNGO, has released a 60-page guide to help companies select safer concern. A web-based tool, Clean Production Action's GreenScreen, enables companies to evaluate 18 potential problems related to chemical selection such as carcinogenicity, human reproduction-related issues, or possibility of ecosystem damage. The guide is advanced partially to provide information relating to the safety of chemicals and address the concern of consumers. The strategies and resources offered to companies through this publication are expected to assist the implementation of safer chemical use principles.

(30) Development of GSK's reagent guides – embedding sustainability into reagent selection: ***Green Chem.***, 2013,**15**, 1542. **DOI:** 10.1039/C3GC40225H

Reagent guides ranking commonly used reagents for 15 transformations have been developed to reduce the environmental impact of drug discovery and development. Reagents have been scored by a combination of health, safety and environmental risk phrases, life cycle analysis (where possible) and an assessment of the chemistry including considerations of atom efficiency, stoichiometry, work-up and other issues. Guides covering alkene reduction, amide formation, C–H bromination, C–H chlorination, deoxychlorination, epoxidation, ester formation, ether formation, fluorination, iodination, ketone reduction, nitro reduction, oxidation of alcohols to aldehydes and ketones, reductive amination and sulfur oxidation are shared, with an explanation of the methodology behind their generation.

GSK Reagent Selection Guide – Amide Formation



Few Issues
Enzyme
Activated silica
CDI
COMU®

Some Issues
i-BuOCOCl
Ghosez reagent
Mukaiyama reagent
SuOCOOSu
TFFH
EEDQ
Thionyl chloride
EDCI (WSCDI)
T3P®
Oxalyl chloride
CDMT

Major Issues
PyBOP®
TBTU
DCC
DPPA
Boric Acid
Cyanuric chloride
HOBt
DMTMM
HBTU
DIC
HATU
HOAt

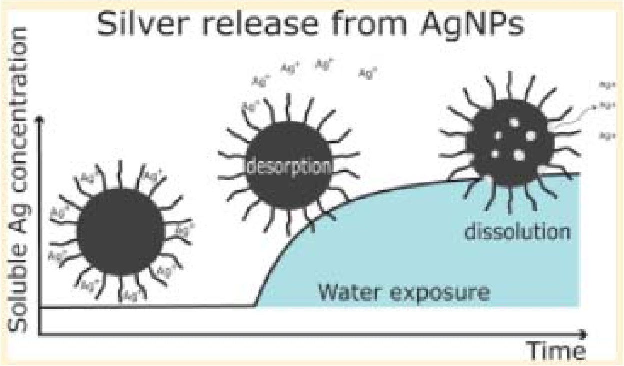
IV. Toxicity Arising from Applying Nanomaterials and Nanotechnology:

(31) <u>Editorial: Environmental Health and Safety Considerations for Nanotechnology:</u> **Chem. Rev.**, 2013, **46**, 605. For your reference, in this special issue, there are 26 related articles.

An important conceptual advance in nanotechnology environmental and health (nano-EHS) assessment has been the recognition that the dynamic physicochemical properties of engineered nanomaterials (ENMs) play a key role in their fate and transport, human and environmental exposure, and hazard generation. Thus, it is imperative to develop robust *in vitro* and *in vivo* safety assessment approaches that relate specific material properties to possible mechanisms of biological injury, pathophysiology of disease, dosimetry, and exposure of humans and environment life forms. This requires critical knowledge acquisition about the unique interactions of organic, inorganic, and hybrid ENMs, as well as the commercial nanocomposites and derivative materials at the nano/bio interface, including the use of this information to establish structure–activity relationships (SARs) and risk reduction strategies. We have come to recognize that, because of the diverse and unique properties of ENMs, safe implementation of nanotechnology and the governance of nano-EHS is a multidisciplinary exercise that goes beyond traditional hazard, exposure, and risk assessment strategies. This requires cooperation between academia, industry, government, and the public to allow for the proper coordination of nano-EHS activities, rational decision-making tools, and the development of sustainable technology approaches. These processes could be accelerated by implementation of predictive toxicological approaches and rapid throughput screening platforms, as well as exploiting computational methods to assist in the establishment of quantitative SARs and safer-by-design approaches. While basic knowledge is being gathered, it is important to develop appropriate incremental regulatory approaches for safe nano-EHS implementation and advancement of materials to the marketplace with public acceptance and support.

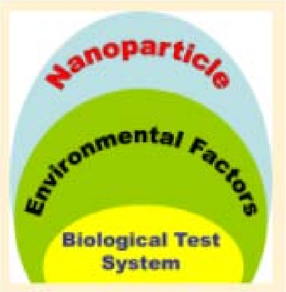
(32) Silver release from silver nanoparticles in natural water: *Environ. Sci. Technol.*, **2013**, *47*, 4140. **DOI:** 10.1021/es304023p

Silver Release from **Silver Nanoparticles** in **Natural** Waters ... Spherical **silver nanoparticles** of various sizes and surface coatings were considered in this study: 5 and 50 nm PVP-coated AgNPs (6.5 ± 0.8 and 53.4 ± 5.0 nm), 5 and 50 nm Tan-coated AgNPs (4.3 ± 1.3 and 52.1 ± 7.1 nm), and 10 and 50 nm Cit-coated AgNPs (8.2 ± 1.2 and 49.1 ± 4.5 nm) were obtained from nanoComposix (San Diego, CA) as suspensions in **water** (20 mg/L) and characterized by transmission electron microscopy (TEM) and dynamic light scattering (DLS) (see Figures S1 and S2 of the Supporting Information).



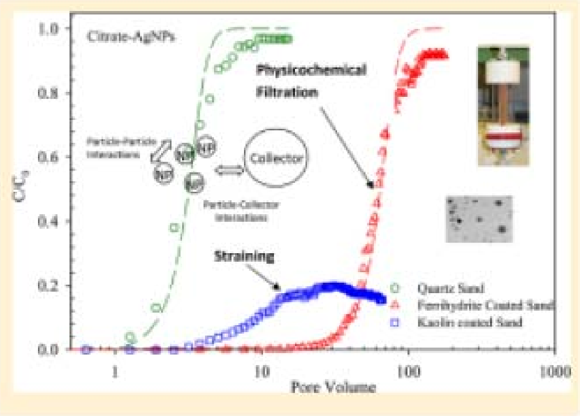
(33) Effect of Nanoparticle Stabilization and Physicochemical Properties on Exposure Outcome: Acute Toxicity of Silver Nanoparticle Preparations in Zebrafish (*Danio rerio*): ***Environ. Sci. Technol.***, 2013, ***47***, 3883. **DOI:** 10.1021/es303695f

Nanotechnology has vast potential for expanded development and novel application in numerous sectors of society. With growing use and applications, substantial production volumes and associated environmental release can be anticipated. Exposure effect of nanoparticles (NP) on biological systems may be intrinsic to their physicochemical properties introducing unknown associated risk. Herein, we expand the knowledge of health and environmental impact of silver nanoparticles (AgNPs), testing the **acute toxicity** of 14 AgNP preparations on developing zebrafish embryos (*Danio rerio*). Toxicological end points, including mortality, hatching rate, and heart rate were recorded. Concentration, stabilization agent and physicochemical properties were monitored as contributing outcome factors. Our findings indicate wide ranging LC_{50} 24 h postfertilization values (0.487 ppm (0.315, 0.744 95% CI) to 47.89 ppm (18.45, 203.49 95% CI)), and indicate surface charge and ionic dissolution as key contributory factors in AgNP exposure outcome.



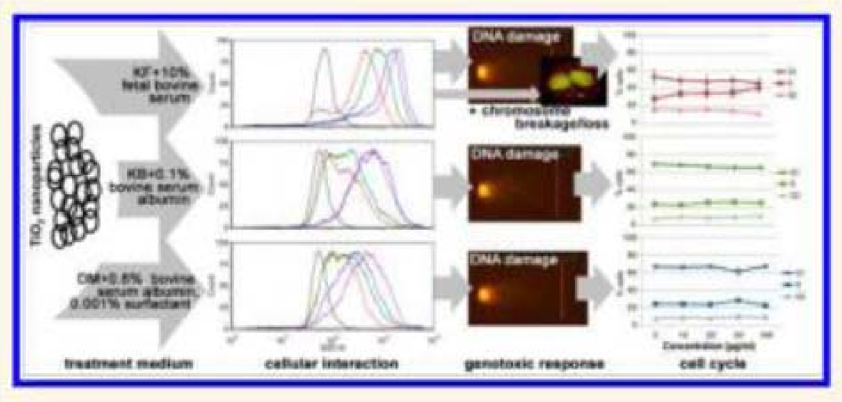
(34) Key Factors Controlling the Transport of Silver Nanoparticles in Porous Media : ***Environ. Sci. Technol.***, 2013, **47** , 4039. **DOI:** 10.1021/es304580r

The current study investigated the mobility of four silver nanoparticles (AgNPs) stabilized using different capping agents and represent the common stabilization mechanisms as well as surface charging scenarios in reactive and nonreactive porous media. The AgNPs were (1) uncoated H_2-AgNPs (electrostatically stabilized) and (2) citrate coated AgNPs (Citrate-AgNPs) (electrostatically stabilized), (3) polyvinylpyrrolidone coated AgNPs (PVP-AgNPs) (sterically stabilized), and (4) branched polyethyleneimine coated AgNPs (BPEI-AgNPs) (electrosterically stabilized). The porous media were (1) quartz sand (QS), (2) ferrihydrite-coated sand (FcS), and (3) kaolin-coated sand (KcS). The H_2-AgNPs and Citrate-AgNPs were readily mobile in QS but significantly retained in FcS and KcS with more deposition achieved in the KcS media. The deposition of the H_2-AgNPs and Citrate-AgNPs followed the order of KcS > FcS > QS. The PVP-AgNPs breakthrough occurred more rapid as compared to the H_2-AgNPs and Citrate-AgNPs but the deposition of PVP-AgNPs followed the same order of the electrostatically stabilized AgNPs (KcS > FcS > QS). The BPEI-AgNPs were readily mobile regardless of the porous media reactivity. Physicochemical interactions were the dominant filtration mechanism in the majority of the investigated cases but straining played the major role in the deposition of the electrostatically stabilized H_2-AgNPs and Citrate-AgNPs in the KcS media. The results highlight the importance of both the stabilization mechanism and capping agent chemistry as key factors governing the transport of AgNPs in the environment.



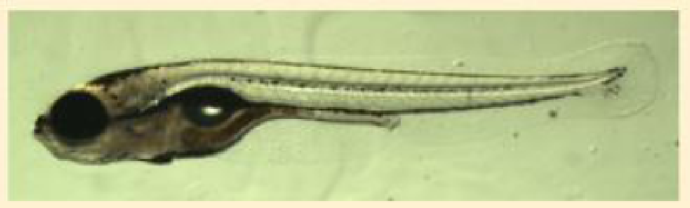
(35) Effect of Treatment Media on the Agglomeration of Titanium Dioxide Nanoparticles: Impact on Genotoxicity, Cellular Interaction, and Cell Cycle: *ACS Nano*, **2013**, *7* , 1929. **DOI:** 10.1021/nn302280n

The widespread use of titanium dioxide (TiO_2) nanoparticles in consumer products increases the probability of exposure to humans and the environment. Although TiO_2 nanoparticles have been shown to induce DNA damage (comet assay) and chromosome damage (micronucleus assay, MN) *in vitro*, no study has systematically assessed the influence of medium composition on the physicochemical characteristics and genotoxicity of TiO_2 nanoparticles. We assessed TiO_2 nanoparticle agglomeration, cellular interaction, induction of genotoxicity, and influence on cell cycle in human lung epithelial cells using three different nanoparticle-treatment media: keratinocyte growth medium (KGM) plus 0.1% bovine serum albumin (KB); a synthetic broncheoalveolar lavage fluid containing PBS, 0.6% bovine serum albumin and 0.001% surfactant (DM); or KGM with 10% fetal bovine serum (KF). The comet assay showed that TiO_2 nanoparticles induced similar amounts of DNA damage in all three media, independent of the amount of agglomeration, cellular interaction, or cell-cycle changes measured by flow cytometry. In contrast, TiO_2 nanoparticles induced MN only in KF, which is the medium that facilitated the lowest amount of agglomeration, the greatest amount of nanoparticle cellular interaction, and the highest population of cells accumulating in S phase. These results with TiO_2 nanoparticles in KF demonstrate an association between medium composition, particle uptake, and nanoparticle interaction with cells, leading to chromosomal damage as measured by the MN assay.



(36) TiO_2 Nanoparticle Exposure and Illumination during Zebrafish Development: Mortality at Parts per Billion Concentrations: *Environ. Sci. Technol.*, **2013**, *47*, 4726. **DOI:** 10.1021/es304514r

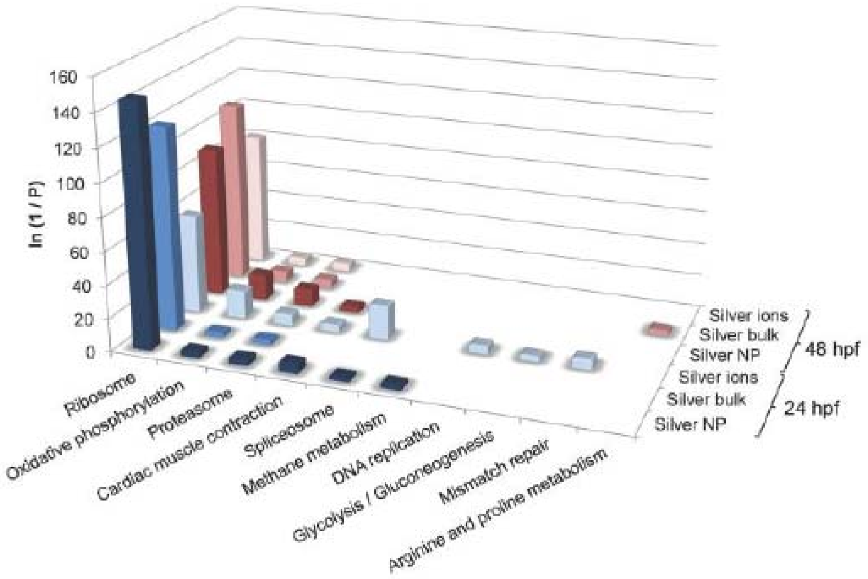
Photoactivation of titanium dioxide nanoparticles (TiO_2NPs) can produce reactive oxygen species (ROS). Over time, this has the potential to produce cumulative cellular damage. To test this, we exposed zebrafish (*Danio rerio*) to two commercial TiO_2NP preparations at concentrations ranging from 0.01 to 10 000 ng/mL over a 23 day period spanning embryogenesis, larval development, and juvenile metamorphosis. Fish were illuminated with a lamp that mimics solar irradiation. TiO_2NP exposure produced significant mortality at 1 ng/mL. Toxicity included stunted growth, delayed metamorphosis, malformations, organ pathology, and DNA damage. TiO_2NPs were found in the gills and gut and elsewhere. The two preparations differed in nominal particle diameter (12.1 ± 3.7 and 23.3 ± 9.8 nm) but produced aggregates in the 1 μm range. Both were taken up in a dose-dependent manner. Illuminated particles produced a time- and dose-dependent increase in 8-hydroxy-2′-deoxyguanosine DNA adducts consistent with cumulative ROS damage. Zebrafish take up TiO_2NPs from the aqueous environment even at low ng/mL concentrations, and these particles when illuminated in the violet-near UV range produce cumulative toxicity.



(37)Molecular mechanisms of toxicity of silver nanoparticles in Zebrafish Embryos: ***Environ. Sci. Technol.***, Just Accepted. **DOI:** 10.1021/es401758d

Silver nanoparticles cause toxicity in exposed organisms and are an environmental health concern. The mechanisms of silver nanoparticle toxicity, however, remain unclear. We examined the effects of exposure to silver in nano-, bulk- and ionic forms on…

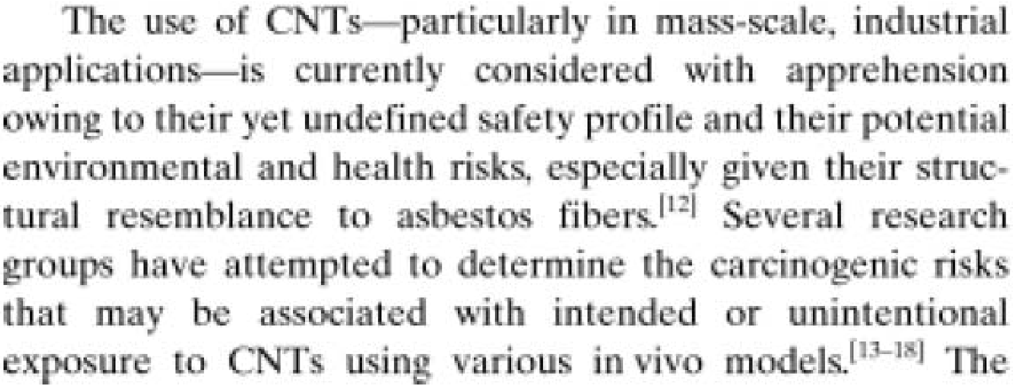
van Aerle et al - Figure 3



(38) Multiwalled Carbon Nanotubes at Environmentally Relevant Concentrations Affect the Composition of Benthic Communities : *Environ. Sci. Technol.*, Article ASAP. **DOI:** 10.1021/es400777j

To date, chronic effect studies with manufactured nanomaterials under field conditions are scarce. Here, we report *in situ* effects of 0, 0.002, 0.02, 0.2, and 2 g/kg multiwalled carbon nanotubes (MWCNTs) in sediment on the benthic community composition after 15 months of exposure. Effects observed after 15 months were compared to those observed after 3 months and to community effects of another carbonaceous material (activated carbon; AC), which was simultaneously tested in a parallel study. Redundancy analysis with variance partitioning revealed a total explained variance of 51.7% of the variation in community composition after 15 months, of which MWCNT dose explained a statistically significant 9.9%. By stepwise excluding the highest MWCNT concentrations in the statistical analyses, MWCNT effects were shown to be statistically significant already at the lowest dose investigated, which can be considered environmentally relevant. We conclude that despite prolonged aging, encapsulation, and burial, MWCNTs can affect the structure of natural benthic communities in the field. This effect was similar to that of AC observed in a parallel experiment, which however was applied at a 50 times higher maximum dose. This suggests that the benthic community was more sensitive to MWCNTs than to the bulk carbon material AC.

(39)Asbestos-like Pathogenicity of Long Carbon Nanotubes Alleviated by Chemical Functionalization: **Angew. Chem. Int. Ed.,** 2013, **52**, 2214.
DOI: 10.1002/anie.210207664



The use of CNTs—particularly in mass-scale, industrial applications—is currently considered with apprehension owing to their yet undefined safety profile and their potential environmental and health risks, especially given their structural resemblance to asbestos fibers.[12] Several research groups have attempted to determine the carcinogenic risks that may be associated with intended or unintentional exposure to CNTs using various in vivo models.[13–18] The

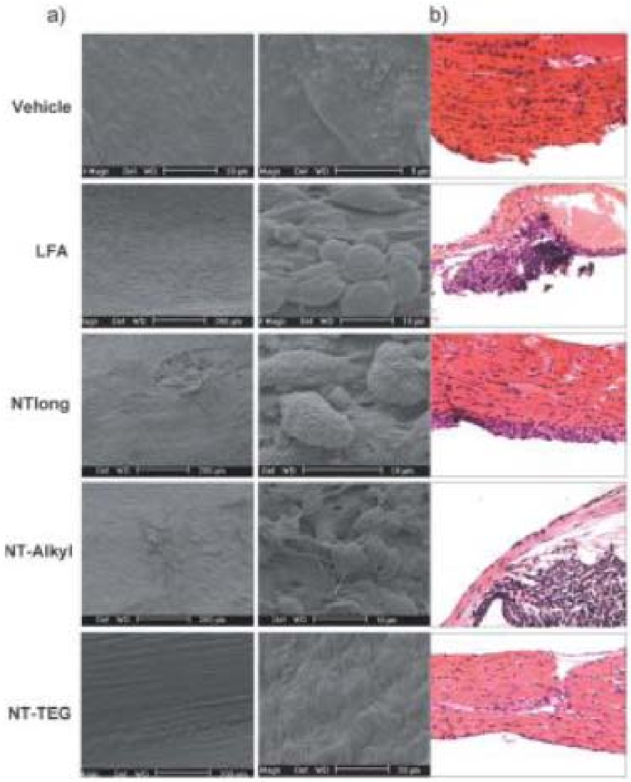
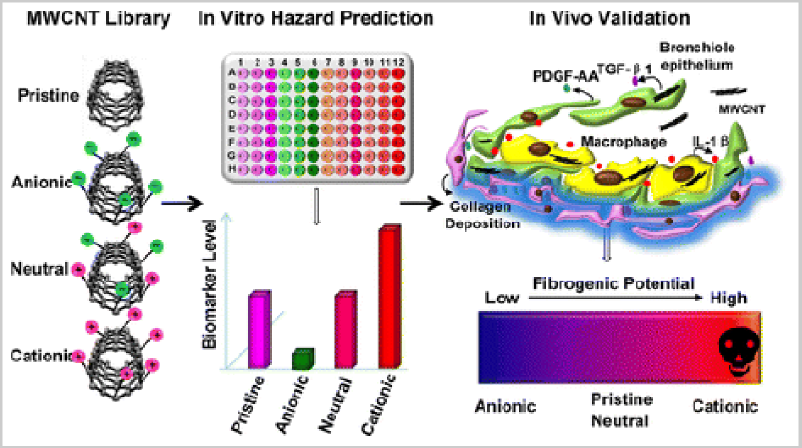


Figure 3. The effect of fibers on the diaphragms after 7 days. Female C57Bl/6 mice were intraperitoneally injected with 50 µg of vehicle control (0.5% BSA/saline), pristine MWNTs (NTlong), the two chemically functionalized MWNTs (NT-Alkyl and NT-TEG), or LFA as a positive control, the mice were killed after 7 days and the diaphragms excised, fixed, and prepared for visualization. a) SEM images of the diaphragm surface and b) histology using H&E staining shows the presence of granulomatous inflammation with NTlong, LFA, and NT-Alkyl but not with NT-TEG. Low and high magnification of the SEM images are shown.

(40)Surface Charge and Cellular Processing of Covalently Functionalized Multiwall Carbon Nanotubes Determine Pulmonary Toxicity: *ACS Nano*, **2013**, *7*, 2352. **DOI:** 10.1021/nn305567s

Functionalized carbon nanotubes (*f*-CNTs) are being produced in increased volume because of the ease of dispersion and maintenance of the pristine material physicochemical properties when used in composite materials as well as for other commercial applications. However, the potential adverse effects of *f*-CNTs have not been quantitatively or systematically explored. In this study, we used a library of covalently functionalized multiwall carbon nanotubes (*f*-MWCNTs), established from the same starting material, to assess the impact of surface charge in a predictive toxicological model that relates the tubes' pro-inflammatory and pro-fibrogenic effects at cellular level to the development of pulmonary fibrosis. Carboxylate (COOH), polyethylene glycol (PEG), amine (NH_2), sidewall amine (sw-NH_2), and polyetherimide (PEI)-modified MWCNTs were successfully established from raw or as-prepared (AP-) MWCNTs and comprehensively characterized by TEM, XPS, FTIR, and DLS to obtain information about morphology, length, degree of functionalization, hydrodynamic size, and surface charge. Cellular screening in BEAS-2B and THP-1 cells showed that, compared to AP-MWCNTs, anionic functionalization (COOH and PEG) decreased the production of pro-fibrogenic cytokines and growth factors (including IL-1β, TGF-β1, and PDGF-AA), while neutral and weak cationic functionalization (NH_2 and sw-NH_2) showed intermediary effects. In contrast, the strongly cationic PEI-functionalized tubes induced robust biological effects. These differences could be attributed to differences in cellular uptake and NLRP3 inflammasome activation, which depends on the propensity toward lysosomal damage and cathepsin B release in macrophages. Moreover, the *in vitro* hazard ranking was validated by the pro-fibrogenic potential of the tubes *in vivo*. Compared to pristine MWCNTs, strong cationic PEI-MWCNTs induced significant lung fibrosis, while carboxylation significantly decreased the extent of pulmonary fibrosis. These results demonstrate that surface charge plays an important role in the structure-activity relationships that determine the pro-fibrogenic potential of *f*-CNTs in the lung



(41)<u>Fate of CuO and ZnO Nano- and Microparticles in the Plant Environment:</u> ***Environ. Sci. Technol.***, 2013, ***47***, 4734. **DOI:** 10.1021/es304736y

The environmental fate of metal oxide particles as a function of size was assessed by comparing the behavior of CuO or ZnO nanoparticles (NPs) to that of the corresponding microparticles (MPs) in a sand matrix, with and without wheat (*Triticum aestivum* L.) growth. After 14 days of incubation in the planted sand, the

CuO and ZnO NPs were increased from their nominal sizes of <50 nm and <100 nm, to ~317 nm and ~483 nm, respectively. Accordingly, the negative surface charge of colloids present in aqueous extracts from the sand amended with CuO (−27.0 mV) and ZnO (−10.0 mV) NPs was reduced by the presence of plants, to −19.8 mV and −6.0 mV, respectively. The surface charge of the MPs was not influenced by plants. Plant growth increased dissolution of NPs and MPs of both metal oxides in the sand from <0.3 mg/kg to about 1.0 mg/kg for the CuO products, and from ≤0.6 mg/kg to between 1.0 and 2.2 mg/kg for the Zn products. The NP or MP products reduced wheat root length by ~60% or ~50% from control levels; CuO was more toxic than ZnO. X-ray absorption spectroscopy (XAS) analysis showed that treatments with MPs or NPs of ZnO led to similar accumulations of Zn-phosphate species in the shoots, likely from dissolution of ZnO. Exposure to CuO NPs or MPs resulted in similar XAS spectra for Cu in the shoots explained by plant accumulation of both CuO and Cu^{I}-sulfur complexes. These findings demonstrate the similarities between commercial NPs and MPs of CuO or ZnO in wheat plants, with greater root toxicity correlating with smaller particle size. Factors from the sand and the plant modified the aggregation or dissolution of both types of particles, thus, influencing their environmental fates.