VOLUME 2 NUMBER 7

The OPCW Science & Technology Monitor

A sampling of Science & Technology Relevant to the Chemical Weapons Convention

1 June 2015

In This Issue

Featured content

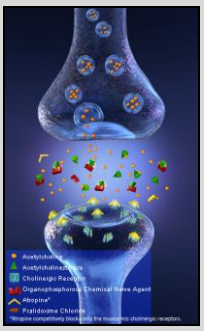


Image from DuoDote®

Medical countermeasures at work in a synapse.

Fingerprinting chemicals.

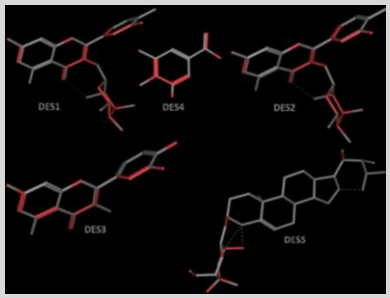


*Image from PLoS One. **2013** Nov, 8(11)*

Drug discovery research in OPCW Supported Research Projects

Welcome

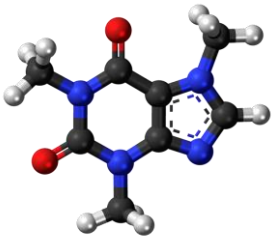
Welcome to the *OPCW Science and Technology Monitor*, an occasional bulletin to provide updates on developments in science and technology across a broad spectrum of topics relevant to the CWC. Past issues are available from the Science and Technology section of the OPCW website.

Thanks to all of you who have taken our survey. For those who have not yet responded, the survey is still open (click here). There are only six questions, all easier than the puzzle (we promise) and all responses are anonymous. Your feedback is highly appreciated!

Today marks the 25th anniversary of the signing of the 1990 Chemical Weapons Accord by the United States of America and the Soviet Union. This agreement, which pre-dated the CWC, marks one of many steps taken in the journey toward a world free of chemical weapons. Steps taken in chemical disarmament have been supported by the science of chemistry itself; a scientific field that provides opportunities for international collaborations and brings forth new developments with peaceful economic and technological benefits. As we move into the future, we look forward to a wealth of new discoveries from this evolving scientific field.

The S&T Puzzle

We once again congratulate our colleagues at the CTBTO, whose entry correctly recognized four of the top five spoken words of the Director-General in the eight statements delivered from 22 January to 29 April 2015 (in case you were wondering, they missed "States"). The prize for best visualisation of the words of the Director-General, however, goes unclaimed as no submissions (except our own, below) were received. Puzzle statistics now stand at: VER 4, OSP 2, OCS 1, INS 1 and CTBTO 3.



For this edition of the puzzle, we look at the multiple uses of a cup of coffee. Can you tell us the identity and LD_{50} (that's right, the median lethal dose) of the most abundant chemical in the cup; the molarity (M) of caffeine (molecule above); and the LD_{50} of coffee itself? To keep this simple, assume this coffee is made with Arabica beans and brewed by a certified procedure (for

Science Fun:

As much fun as we have with *Science Fun*, we have found that it is not always fun trying to research and identify suitable material to use in each new issue! So where do inspiration and ideas come from? We've previously seen reports that certain beverages can help (when properly consumed of course); one of our favorites is prepared from a material containing more than 1500 chemicals! With so many chemical components, we needed a part one and a part two of reference articles to describe it! Given the worldwide consumption of this beverage, you are probably already quite familiar with it and its most familiar ingredient, 1,3,7-trimethylxanthine. Are you genetically predisposed to enjoy this beverage? If unsure, you might check these eight loci. If yes, then we invite you to sit down with a cup and learn about the science of coffee (and if no, we won't mind if you choose to drink something more compatible with your personal genome!).

Preparing to draft the next issue of the *S&T Monitor*.

Coffee cultivation covers more than 11 million hectares of the planet! Anything so important requires study in the most advanced laboratory settings, and the study of coffee has revealed a genome that has evolved to produce caffeine and all those aroma producing components! One area of current interest is the economic viability of coffee cultivation in relation to climate change (take example, ISO 6668:2008) and our "cup" holds 250 ml (to ensure we stay below the LD_{50}). The first person to give us the correct answers (highest number of the four questions) wins the prize: a choice of requesting a featured topic, designing a puzzle, or receiving a beverage hand selected by the Science Policy Adviser. Send answers by email. Good luck!

News and Updates

Recent reports and publications:

Presentations (videos and slides) from the Continuing Innovation in Information Technology Workshop (held on 5 March at the National Academy of Sciences, Washington DC, USA).

A look at EU funded projects producing advanced analysis and visualisation tools for archaeology and restoration. Such tools could benefit other types of investigations.

Advances in optical fibres are helping make laser based weapons a reality.

The Epigenome Roadmap, a collection of research papers describing the main findings of the NIH Roadmap Epigenomics Program.

Have you ever wondered how to describe the complexity of a chemical structure and if that complexity description is reduced by advances in synthetic chemistry? Read about a new tool for assessing the "current complexity" of organic molecules.

Which factors influence international mobility of research scientists? Report from OECD.

Report from the workshop on ethical guidelines in the practice of chemistry (held on 11 March at OPCW).

Making It Happen: Technology, Finance and Statistics for Sustainable Development in Asia and the Pacific. Report from UNDP.

Science and education resources:

Card games to learn science: Retrosynthetic Rummy, Ion (use ions to make compounds), Evolve and Linkage (games to explore relationships between RNA and DNA).

POPs Hunter: A Smartphone game to learn about pollutants.

Some news from world of science and technology:

From the weeks of 10 – 16, 17 – 23 and 24-30 May in chemistry.

Spectrometers, magnetometers, thermometers and more. The science instruments of NASA's Europa mission.

The United Nations turns 70 this year. Here's a look at 10 innovative programmes and projects that it has initiated.

for example this study that indicates coffee crop yields would decrease in current regions of production with a global temperature rise). Today, scientists are using big data to develop actionable solutions for the future the world's morning beverage of choice.

For those of us who prefer to drink coffee rather than grow it or manipulate its genome, it is good to recognize the health implications of coffee consumption; although it may be what you take with your coffee that needs to be watched! Did you know that pent coffee grounds are a potential source for bioactive compounds (and also biodiesel)? The issue of water quality and temperature must also be considered when talking about the difference between a good and perfect cup! Like so many of the food and beverages we enjoy, drinking coffee is a sensory experience (especially with espresso), we enjoy the smell and the taste, but what about the sound of coffee? Did you know that roasting coffee is both a chemical and an acoustic process? For those who prefer an espresso to that garden variety cup of coffee, make sure you get these three critical steps correct!

In our world of fancy gadgets, even the tried and true coffee maker has evolved with the times, one was recently installed on the International Space Station (requiring a special zero-gravity cup)! Of course, a cup of coffee can still be produced in a low-tech manner for those in a bind, using three light bulbs and some sandpaper for example. If necessary, a robot can help operate your coffee machine too. Finally, we point out that even coffee making has been assimilated by convergent science and technology: coffee machines have become valuable tools in chemistry laboratories for performing hot-water extractions, just what you need to brew up natural products.

Medical Countermeasures

Critical for response to a chemical attack is access to countermeasures to treat victims and protect emergency responders. The OPCW Scientific Advisory Board has produced reports on treatments for nerve and blister agent exposure; and on adjunct agents and new trends in the treatment of nerve agent poisoning. Despite published recommendations for treatment and availability of countermeasures, a number of limitations and challenges still remain. In this feature we reference recent publications relevant to medical countermeasures to inform interested readers about ongoing work in the field. It is notable that a number of these reports make reference to events in the Syrian Arab Republic from 2013.

Starting with countermeasures to organophosphorus poisoning, there are the familiar autoinjectors that contain atropine and an oxime (such as obidoxime, pralidoxime, TMB-4 or HI-6); as effectiveness can vary with the nerve agent of exposure, we have seen studies to identify additional oximes. The autoinjector is designed to deliver antidotes to muscle where the primary effect of the nerve agent occurs, however, nerve agent exposure can also produce neurodegenration. For mitigation of neurodegeneration, anticonvulsants are combined with atropine and oximes; typically diazepam, lorazepam or midazolam (and a number of other suitable substances have been reported). The psychoactive drug ketamine, may also have neuroprotective benefits (and has been studied for controlling epileptic seizures). Oximes that can cross the blood-brain-barrier and provide neuroprotective benefits continue to be an active area of study.

The enzyme butyrylcholinesterase can be used to scavenge nerve agents and prevent inhibition of acetylcholinesterase (a "bioscanvenger"). Combinations of butyrylcholinesterase with oximes have been studied to enable catalytic bioscavenging (studies have also been conducted using acetylcholinesterase mutants), while other approaches involve combining bioscavengers with hyaluronan-degrading enzymes. Modified cyclodextrins have also been proposed as potential catalytic scavengers.

Pre-treatments to nerve agent exposure that rely on carbamates or topical skin protectants are also known (see for example these studies on the effectiveness of topical protectants against VX and soman). As pre-treatments must be applied before exposure; emergency responders would need to recognize nerve agent presence prior to deployment (in this context, it has been suggested that social media could be used as a tool to help evaluate clinical syndromes). Research continues on additional options for supplementary drug treatments and possible alternatives to atropine and oximes.

Therapeutic strategies for sulphur mustard exposure have focused on anti-inflammatory compounds, antioxidants, protease inhibitors and antiapoptotic compounds. Combination anti-inflammatory and anti-cholinergic skin treatments have also

Crowdsourcing:

Map the 3D neural circuits that make vision possible by playing a game. With 84 million neurons in a human brain, your help really is needed!

Do you have clever designs for 3D printed objects? Are you a student? Do you live in India? Yes, yes, and yes? Then take a look at this 3D Printing Design contest.

Interested in education and outreach to build public awareness and involvement in protecting water resources? Participate in the World Water Monitoring Challenge™ (a truly global crowdsource as can be seen by the data collected thus far).

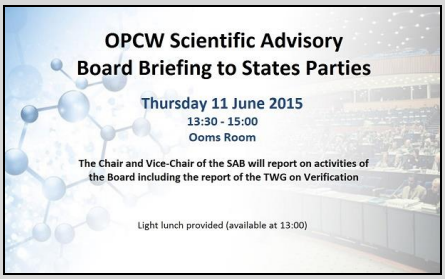
Crowdsourcing the world for emergency medicine – insights from two recent studies.

Upcoming S&T Related Events:

OPCW Calendar of Events June to December 2015.

7 – 12 June 2015
2015 AAAS-TWAS Course on Science Diplomacy.
Trieste, Italy.

8 – 12 June 2015
Twenty-Second Session of the OPCW Scientific Advisory Board.
OPCW Headquarters, The Hague, Netherlands.



22 – 26 June 2015
CTBT Science and Technology Conference (SnT2015)
Vienna, Austria.

show therapeutic potential. Other treatments of interest include the use of the catalytic antioxidant AEOL 10150, a compound previously studied for treatment of chlorine gas inhalation, as a possible countermeasure against sulphur mustard skin exposure. The peptide Rlip76, known to reduce oxidative stress in cells, may also have countermeasure potential as seen in a recent patent application. Finally, tissue plasminogen activator (tPA) can help to prevent airway obstruction (a possible consequence of sulphur mustard exposure). For topical treatments, fatty acids and cholesterol have been studied as a means to modulate skin adsorption.

While we've focused on nerve and blister agents, as there are far too many agents and countermeasures for a comprehensive review, the following reports may also be of interest: nitrocobinamide as an anti-cyanide antidote, antibodies that inhibit the transport of Ricin in cells and the use of polymers as antidotes for toxins.

Chemical Forensics

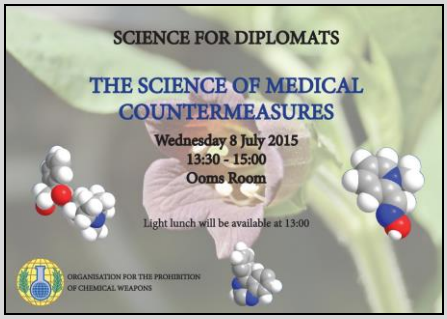
We thank our colleagues from the OPCW Laboratory for their major contribution and input to this feature

The ability to obtain unique signatures such as fingerprints and DNA to identify individuals or the marks left on a fired bullet to identify the firearm that shot it, to compare with reference materials (such as a fingerprint obtained from a suspect) are among the most powerful forensic tools available to law enforcement. Chemical signatures that indicate drug use or gender can even be collected from fingerprints.

Chemical samples can also have unique signatures that might reflect how and where they originated. For the Chemical Weapons Convention, one might ask, questions such as: What kind of molecular signatures exists for chemical warfare agents and toxic chemicals that may have been used in an incident under investigation, what kind of reference samples are required for comparison and what kind of forensic information can be obtained with such information?

Impurity profiling is the determination of types and quantities of impurities within a chemical sample (a type of analysis with important pharmaceutical and illicit drug law enforcement related applications). As molecules are made up of atoms of different elements connected in a specific way by chemical bonds it is tempting to think that this cannot be the source of a unique signature that could allow tracing back the origin of the chemical. However, chemicals are almost never absolutely pure. That is they contain impurities, which in the case of toxic chemicals and warfare agents, might be: side products of the reaction that produced the toxic chemical; side products originating from earlier reactions leading to precursors used to produce the toxic chemical; intermediate and final products of degradation reactions; and/or additives and stabilizers deliberately added to a toxic chemical.

8 July 2015
"Science for Diplomats". The science of medical countermeasures.
13:30 – 15:00 Ooms Room
OPCW Headquarters, The Hague, Netherlands.



14 – 26 July 2015
19th Annual Green Chemistry and Engineering Conference.
Bethesda, ML, USA.

19 – 22 July 2015
12th World Congress on Industrial Biotechnology.
Montreal, Canada.

6 – 13 August 2015
IUPAC 2015
48th IUPAC General Assembly and 45th World Chemistry Congress.
Busan, Republic of Korea

10 - 14 August 2015
Biological Weapons Convention Meeting of Experts.
Geneva, Switzerland.

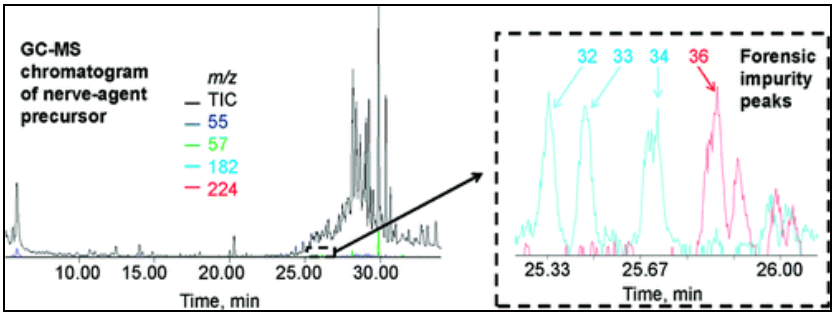
16 – 20 August 2015-05-25
250th American Chemical Society National Meeting and Exhibition.
Boston, MA, USA.

31 August – 4 September 2015
Sixth Summer Programme on Disarmament and Non-Proliferation of Weapons of Mass Destruction (WMD) in a Changing World. Asser Institute, The Hague, The Netherlands.

27 September – 1 October 2015
ECCE10 (10th European Congress of Chemical Engineering); ECAB3 (3rd European Congress of Applied Biotechnology); and EPIC5 (5th European Process Intensification Conference)
Nice, France.

The chemicals that constitute the impurities can be indicative of the source of the chemical, the location from where it was collected, the process used to prepare or purify the chemical, or even a unique preparation (batch) of the chemical sample.

In addition to the presence of the impurities themselves, their relative amounts constitute another important signature. Some impurities will be stable under storage or reaction conditions or even in the environment after a chemical agent has been deployed, others will react further to produce other chemicals. "Stable" impurities are of high value for a signature as they potentially carry information from different steps in the preparation process. In situations where the sample is a mixture of several chemicals (or isomers of a given chemical), ratios of components can also be informative.



Impurity Profiling of a Nerve Agent from Researchers at the Pacific Northwest National Laboratory (Figure Copyright © 2011 American Chemical Society).

Most (but not all) chemical elements are composed of more than one stable (that is non-radioactive) isotope. For example carbon exists as two stable isotopes, ^{12}C (carbon with an atomic mass of 12) and ^{13}C (carbon with a mass of 13). On average, there will be 98.93% ^{12}C and 1.07% ^{13}C. However this ratio is not constant and will vary slightly in the environment. The range for ^{12}C is from 98.85% to 99.04% and that for ^{13}C 0.96% to 1.15%. This ratio of stable isotopes, which can be measured using a special (isotope ratio) mass spectrometer, can be used as a molecular signature. Stable isotope analysis can potentially be used to identify the source or supplier of certain chemical compounds. In drug forensics, stable isotope ratios have been successfully used to determine geographical origins of plant derived drugs such as heroin and cocaine. There are also applications in authentication of foods with protected designation of origin. This type of information can be valuable in conjunction with other information on proliferation channels and resource networks.

A significant challenge in chemical forensic analysis is the availability of appropriate reference materials for comparison. The exact nature of the required reference materials depends on the question that is being asked. If a unique molecular signature is used to confirm the origin of a chemical, known samples from the same origin are necessary for comparison; to link a toxic agent with a production batch requires that a sample of this batch is available; to link a chemical agent to certain precursors, reference samples of the precursors must be

5 - 8 October 2015
SOLVE.
Cambridge, MA, USA.

15 October 2015
Smart Manufacturing Summit.
Livermore, California, USA.

31 October - 2 November 2015
The Port Hackathon.
CERN

16 – 19 November 2015
Malta Conference.
Rabat, Morocco.

18 – 21 November 2015
16th Asian Chemical Congress.
Dhaka, Bangladesh.

22 – 27 November 2015
2nd African Conference on Research in Chemical Education (ACRICE)
University of Venda,
Thohoyandou, South Africa.

15 – 20 December 2015
Pacifichem 2015.
Honolulu, Hawaii, USA.

Contact Us:

Questions, ideas, comments, suggestions, want to make a contribution, or be added to the mailing list? Please contact us through the OPCW Office of Strategy and Policy (OSP).

For more frequent updates, Visit us on the web or follow us on Twitter at @OPCW_ST.

available; similarly to show that the same agent from the same batch was used in incidents at several locations, samples from all of these locations must be obtained and compared. Without the availability of the right reference samples the possible information that can be obtained from the determination of chemical signatures can be severely limited. One possible (but not absolute) exception is that it an impurity pattern can indicate a certain type of production process. This need for suitable reference sets for attribution of samples is quite evident in other forensic analysis as well, microbial forensics for example. Furthermore, inhomogeneous chemical profiles across samples can limit the ability to establish links between them.

Impurity profiling and stable isotope analysis are important techniques in law enforcement, as illustrated by many of the references presented. However, chemical forensics as applied to chemical warfare agents is still an area of active and on-going research, not a set of routine techniques. In regard to warfare agents, we have presented a number of proof-of-principle references. To our knowledge there are no reports involving the use of these methods for investigation of warfare agents in an actual case study. We will report on future developments in the field as they come to our attention.

OPCW Research Projects Support Programme

Guest contribution from our colleagues in the International Cooperation Branch

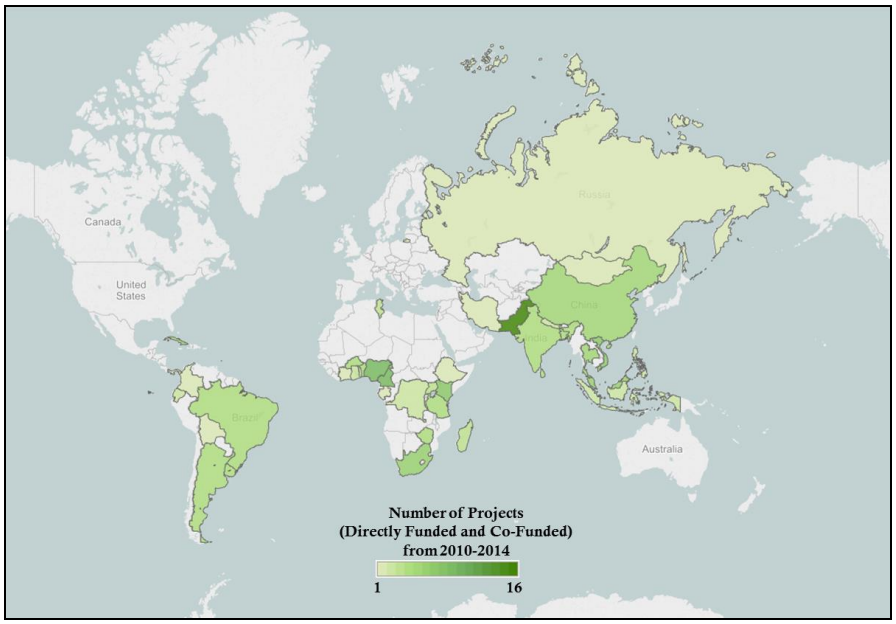


Figure 1: Funded and co-funded research projects through the OPCW Research Project Support Programme from 2010 – 2014.

Chemistry as a scientific discipline has always been central to the Convention. As the destruction of declared stockpiles of chemical weapons moves closer to its conclusion, the work of the OPCW in promoting research, as well as economic and technological development in the field of chemistry, becomes even more important. By supporting scientific research, the OPCW seeks to balance the numerous obligations that the Convention imposes on its Member States and their chemical industries.

For the last 15 years, the OPCW has been supporting small-scale research projects to Member States of the OPCW who fall under the category of developing countries or countries with economies in transition. These projects receive funds to cover auxiliary expenditures, such as consumables, maintenance, and small labware, with the aim of promoting research in the peaceful applications of chemistry hence contributing to economic and technological development of the recipient countries. Figure 1 illustrates the projects that have been funded (both directly and as a cofounder with the International Foundation for Science, IFS) from 2010 – 2014. For more information on the programme and how to apply, see Note S/1258/2015 available on the OPCW public website.

The projects funded from 2010–2014 have been distributed across the African, Asian, and the Latin American and Caribbean group (GRULAC) regions (and a single project was also funded in Eastern Europe) as indicated in Figure 1. Figure 2 illustrates the gender make up of the principle investigators and Figure 3 the areas of research focus.

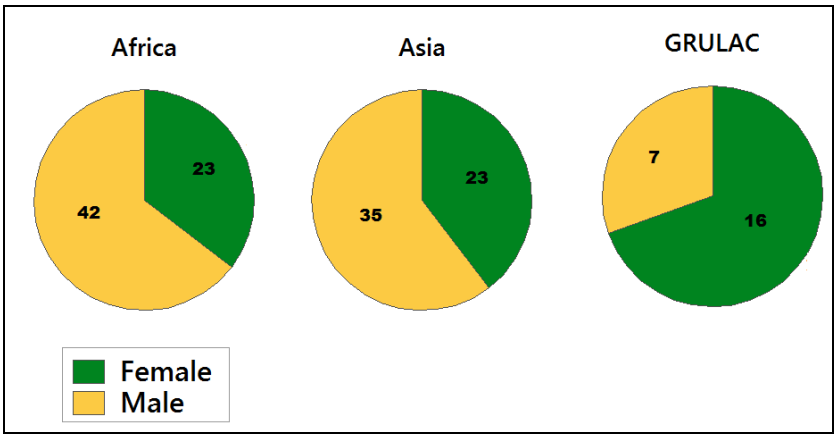


Figure 2: Gender make up of principle investigators in projects funded from 2010-2014.

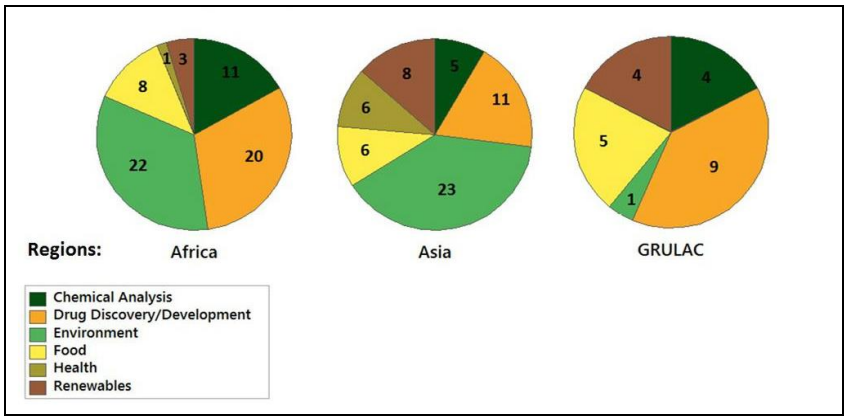


Figure 3: Areas of focus for research projects funded from 2010-2014.

Green chemistry represents an additional dimension to the research areas illustrated in Figure 3. The principles of this field give rise to innovative chemical transformations with high industrial interest and low environmental impact; low toxicity to humans; sustainable uses of energy and resources; and other social and economic sustainability benefits. Clean up and destruction of toxic materials, new analytical methods, reduction of the use and presence of toxic chemicals, and scientific collaborations that result from work in Green Chemistry compliments the core activities of the OPCW (destruction of chemical weapons, non-proliferation, assistance and protection from toxic chemicals, and international cooperation).

The 2010-2014 funding period saw 57 scientific publications go to print in a variety of peer reviewed scientific journals. For those interested in receiving OPCW funding through this programme, the areas noted below (and Green Chemistry projects falling under all of these thematic areas) are of particular interest.

Chemical Analysis: analysis, characterization, and detection of chemicals, including and modelling distributions of measured chemicals in the environment. Recent publications:

- *Confined gold nanoparticles enhance the detection of small molecules in label-free impedance aptasensors*
- *Spatial Variation and Source Distribution of Organic Contaminants in Langat River Basin, Malaysia Using Chemometric Techniques*
- *Structure-fragmentation relationship and rapid dereplication of Buxussteroidal alkaloids by electrospray ionization-quadrupole time-of-flight mass spectrometry*

Drug Discovery: drug design (including *in silico*), drug synthesis and bioactivity of natural substances (*in vitro* and *in vivo*); and, **Health**: medical treatments, prophylactics, protection and the health effects of chemicals. Recent publications:

- *New Antimalarial Hits from Dacryodes edulis (Burseraceae) - Part I: Isolation, In Vitro Activity, In Silico "drug-likeness" and Pharmacokinetic Profiles*
- *Oxindole Derivatives: Synthesis and Antiglycation Activity*
- *Solid-Phase Total Synthesis of Cherimolacyclopeptide E and Discovery of More Potent Analogues by Alanine Screening*

Environmental: pollution monitoring; destruction, remediation, detoxification and prevention; and, health effects of pollutants on humans and ecosystems. Recent publications:

- *Composite nanofloral clusters of carbon nanotubes and activated alumina: An efficient sorbent for heavy metal removal*
- *Nickel and manganese release in serpentine soil from the Ussangoda Ultramafic Complex, Sri Lanka*
- *Pesticide potential dermal exposure during the manipulation of concentrated mixtures at small horticultural and floricultural production units in Argentina: The formulation effect*
- *Structural characteristics and flammability of fire retarding EPDM/layered double hydroxide (LDH) nanocomposites*

Food: chemicals and organisms that have impact and improve food (crops and livestock) production. A recent publication:

- *Chemical Composition and Phenolic Compound Profile of Mortiño (Vaccinium floribundum Kunth)*

Renewables: biomass and natural substances for chemicals and energy. A recent publication:

- *Development of novel in situ nickel-doped, phenolic resin-based micro–nano-activated carbon adsorbents for the removal of vitamin B-12*

Did You Know?

Atropine, a nerve agent countermeasure, was isolated from *atropa belladonna*?