

10 September 2009

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## **Chem-Bio News – S&T Edition**

**1. PROPOSAL FOR SELECTIVE DIFFERENTIATING OF NERVE AGENT G AND V TYPE WITH UTILISATION OF MODIFIED ELLMAN'S METHOD:** *“The procedure for a gradual analysis of G and V type, Sarin, Cyclohexylsarin, Soman, Tabun, agent VX and R-33 was proposed in terms of studied nucleophilic substitution reactions quantification results.”*

**2. A SLIDE SHOW FOR DRUG DISCOVERY:** *“UK scientists have developed a hydrogel slide for monitoring interactions between small molecules and proteins. The slide is an improvement on commercially available slides and could improve drug discovery, they claim.”*

**3. WORLDWIDE ISOTOPE SHORTAGE CONTINUES TO POSE SIGNIFICANT CHALLENGES:** *“According to the survey, 60 percent of radiopharmacies have been impacted by the most recent shortage. Technetium-99m is a product of Molybdenum-99, which has been in short supply recently.”*

**4. HYBRID NANO MATERIAL TARGETS ANTIBIOTIC RESISTANT BACTERIA:** *“German researchers have developed a hybrid, light activated nanomaterial that can target, label and kill harmful antibiotic resistant bacteria such as Escherichia coli.”*

**5. SOLID SUPPORTED LIQUID-LIQUID EXTRACTION OF CHEMICAL WARFARE AGENTS AND RELATED CHEMICALS FROM WATER:** *“The limits of detection of non-toxic analogues of CWAs, and toxic sarin and Lewisite-III, in selected ion monitoring and full scan mode, varied from 0.01 to 0.5  $\mu\text{g mL}^{-1}$  and 0.1 to 1.0  $\mu\text{g mL}^{-1}$  respectively..”*

**6. QUANTITATION OF CHEMICAL WARFARE AGENTS USING THE DIRECT ANALYSIS IN REAL TIME (DART) TECHNIQUE:** *“Furthermore, this study shows that averaging as few as three measurements for each data point is sufficient to produce high quality calibration curves, thus reducing data collection time and providing quicker results..”*

**7. PULMONARY INFLAMMATION TRIGGERED BY RICIN TOXIN REQUIRES MACROPHAGES AND IL-1 SIGNALING:** *“Furthermore, IL1Ra/anakinra cotreatment inhibited ricin-mediated inflammatory responses, including recruitment of neutrophils, expression of proinflammatory genes, and histopathology.”*

# CB Daily Report

## *Chem-Bio News*

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### **PROPOSAL FOR SELECTIVE DIFFERENTIATING OF NERVE AGENT G AND V TYPE WITH UTILISATION OF MODIFIED ELLMAN'S METHOD**

Energy & Ecology

September 11, 2009

"We studied issues of organophosphorus agents' analysis. Immobilised enzyme-inhibitors complexes (e.g. acetylcholinesterase-organophosphate nerve agent) were studied with modified Ellman's biochemical method utilised for assessment of acetylcholinesterase activity."

"Biochemical reactions are widespread and they are the most frequent used analytical methods for determination of nerve agents. This modified method is based on the nucleophilic reactions of mono- and bispyridinium aldoximes of a type 2-PAM, MMB-4 and HI-6, their homologues and isomers with enzyme-inhibitor complexes. The procedure for a gradual analysis of G and V type, Sarin, Cyclohexylsarin, Soman, Tabun, agent VX and R-33 was proposed in terms of studied nucleophilic substitution reactions quantification results. This method enables selective determination of these chemical warfare agents. A gradual analysis was evaluated by statistic method of probabilistic calculus."

The full article can be found at: (M. Hoskovcova, et. al., "Proposal for selective differentiating of nerve agent G and V type with utilisation of modified Ellman's method". Environmental Chemistry Letters, 2009; 7(3):277-281). Link not available.

ANALYST NOTE: The author's contact information is: M. Hoskovcova, National Def University, NBC Def Institute, Vita Nejedleho 68201, Vyskov, Czech Republic.

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### **A SLIDE SHOW FOR DRUG DISCOVERY**

By Emma Shiells

Highlights in Chemical Technology

September 08, 2009

"UK scientists have developed a hydrogel slide for monitoring interactions between small molecules and proteins. The slide is an improvement on commercially available slides and could improve drug discovery, they claim.

Microarrays are used for high throughput studies of molecular interactions. For example,

scientists have immobilised small molecules as spots on 2D slides then probed them with a fluorescently labelled target protein to try to find new drug candidates. But detecting the fluorescent signals is difficult because the interactions are weak and only a small number of molecules can be attached to the slides.

Now David Spring, at the University of Cambridge, and colleagues have made a 3D slide by covering a glass slide with a polyethylene glycol-based hydrogel. Because the 3D slide has a greater surface area than previous 2D slides, more small molecules can be attached to the hydrogel surface.

Spring compared his slide with a commercially available 3D polymer-coated slide. He functionalised both slides with biotin and used fluorescently labelled avidin as the probe protein. The hydrogel slide had a loading capacity an order of magnitude greater than the polymer slide and showed on average a six-fold higher fluorescent intensity."

The full article can be found at: [http://www.rsc.org/Publishing/ChemTech/Volume/2009/11/slide\\_show\\_drug\\_discovery.asp](http://www.rsc.org/Publishing/ChemTech/Volume/2009/11/slide_show_drug_discovery.asp)

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## **WORLDWIDE ISOTOPE SHORTAGE CONTINUES TO POSE SIGNIFICANT CHALLENGES**

Physorg.com

September 08, 2009

"SNM (Society of Nuclear Medicine) recently conducted a survey of nuclear pharmacies—pharmacies that supply the critical radioisotope Technetium-99m, which is used in more than 16 million nuclear medicine tests each year in the United States—to assess, anecdotally, the impact of the worldwide medical isotope shortage. According to the survey, 60 percent of radiopharmacies have been impacted by the most recent shortage. Technetium-99m is a product of Molybdenum-99, which has been in short supply recently."

"Nuclear physicians and pharmacists are making changes to cope with the shortage, while striving to provide patients with the highest levels of care possible. For example, 75 percent of physicians are rescheduling patient tests by at least one day. In more than one out of three of these cases, tests have been delayed for longer than one month.

"This situation is untenable," said Robert W. Atcher, Ph.D., M.B.A, chair of SNM's Domestic Isotope Availability Task Force. "Nuclear scans and procedures that use Tc-99m are used to detect and diagnose many common cancers and cardiac conditions."

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"In addition to delays, more than 80 percent of nuclear physicians and specialists are decreasing the dosage, which can lead to "longer exposure and less effective imaging scans," added Atcher."

The full article can be found at: <http://www.physorg.com/news171649770.html>

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## **HYBRID NANO MATERIAL TARGETS ANTIBIOTIC RESISTANT BACTERIA**

By James Urquhart

Chemistry World

September 08, 2009

"German researchers have developed a hybrid, light activated nanomaterial that can target, label and kill harmful antibiotic resistant bacteria such as Escherichia coli. The zeolite-based material may one day play a major role in both diagnosing and treating infectious diseases and possibly cancer, suggests the team.

So-called 'photodynamic therapy' is a well-established technique in which a light source is used to trigger the action of a light-sensitive drug, and is already used to treat cancer and macular degeneration. However, scientists have been eager to develop cheaper therapeutic approaches with more functions. One such approach would be to develop a single nanomaterial that can carry out three important therapeutic jobs in one; that is, selectively target pathogens, label them (for diagnostic purposes) and then kill them.

Now, Cristian Strassert and colleagues at Westfälische Wilhelms-Universität Münster, Germany, have demonstrated that such a material can work in principle, offering exciting possibilities for next generation phototherapy. 'We have shown that it is possible to functionalise zeolite L in such way that we can label bacteria with a green fluorescence and kill them upon irradiation with red light despite their antibiotic resistance,' says Strassert.

Using zeolite L - a microporous molecular sieve - for the basic structure, the team made several modifications to make it tri-functional. In order to target living microorganisms, the team attached amino groups to the outer surface of the zeolite L nanocrystals. To label the cells, they inserted a highly green luminescent dye into the zeolite channels. And lastly, a photosensitiser that forms toxic singlet oxygen ( $^1O_2$ ) when irradiated with harmless red light was added to the surface."

The full article can be found at: <http://www.rsc.org/chemistryworld/News/2009/September/08090902.asp>

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## **SOLID SUPPORTED LIQUID-LIQUID EXTRACTION OF CHEMICAL WARFARE AGENTS AND RELATED CHEMICALS FROM WATER**

Health & Medicine Week

September 14, 2009

"Solid-supported liquid-liquid extraction was optimized to extract the chemical warfare

agents and their non-toxic analogues from water."

"The developed method was compared to the conventionally used liquid-liquid extraction. This method yielded high recoveries (70-80%) of non-toxic analogues of chemical warfare agents and good recoveries (65-75%) of the nerve agent sarin and Lewisite-III."

"The limits of detection of non-toxic analogues of CWAs, and toxic sarin and Lewisite-III, in selected ion monitoring and full scan mode, varied from 0.01 to 0.5  $\mu\text{g mL}^{-1}$  and 0.1 to 1.0  $\mu\text{g mL}^{-1}$  respectively.."

The full article can be found at: (P.K. Kanaujia, et. al., "Solid Supported Liquid-Liquid Extraction of Chemical Warfare Agents and Related Chemicals from Water". *Chromatographia*, 2009; 70(3-4):623-627). Link not available.

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## **QUANTITATION OF CHEMICAL WARFARE AGENTS USING THE DIRECT ANALYSIS IN REAL TIME (DART) TECHNIQUE**

Medical Letter on the CDC & FDA

September 20, 2009

"Direct analysis in real time (DART) is an ion source that permits rapid mass spectrometric detection of gases, liquids, and solids in open air under ambient conditions. It is a unique technology in the field of chemical weapons detectors in that it does not require a vapor pressure, does not require sample preparation, and is nondestructive to the original sample."

"While the DART technique has had success as a first line instrument of detection, there have been lingering doubts over the technique's quantitative reliability and reproducibility. Here, we demonstrate its capability to produce linear calibration curves ( $R^2 = 0.99$  or better) for the nerve agents GA, GB, and VX as well as the blister agent HD. Independently prepared check standards measured against these curves typically have recovery errors less than 3%. We show the DART instrument response to be linear over roughly 3 orders of magnitude."

"Furthermore, this study shows that averaging as few as three measurements for each data point is sufficient to produce high quality calibration curves, thus reducing data collection time and providing quicker results.."

The full article can be found at: (J.M. Niles, et. al., "Quantitation of Chemical Warfare Agents Using the Direct Analysis in Real Time (DART) Technique". *Analytical Chemistry*, 2009; 81(16):6744-6749). Link not available.

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## **PULMONARY INFLAMMATION TRIGGERED BY RICIN TOXIN REQUIRES MACROPHAGES AND IL-1 SIGNALING**

Medical Letter on the CDC & FDA  
September 20, 2009

“Increasing evidence suggests that the inflammatory effects triggered by ricin are responsible for its lethality. We demonstrated previously that ricin administered to the lungs of mice causes death of pulmonary macrophages and the release of proinflammatory cytokines, suggesting macrophages may be a primary target of ricin. Here we examined the requirement for macrophages in the development of ricin-mediated pulmonary inflammation by employing transgenic (MAFIA) mice that express an inducible gene driven by the c-fms promoter for Fas-mediated apoptosis of macrophages upon injection of a synthetic dimerizer, AP20187. Administration of aerosolized ricin to macrophage-depleted mice led to reduced inflammatory responses, including recruitment of neutrophils, expression of proinflammatory transcripts, and microvascular permeability. When compared with control mice treated with ricin, macrophage-depleted mice treated with ricin displayed a reduction in pulmonary IL-1 beta. Employing mice deficient in IL-1, we found that ricin-induced inflammatory responses were suppressed, including neutrophilia. Neutrophilia could be restored by co-administering ricin and exogenous IL-1 beta to IL-1 alpha/beta(-/-) mice. Furthermore, IL1Ra/anakinra cotreatment inhibited ricin-mediated inflammatory responses, including recruitment of neutrophils, expression of proinflammatory genes, and histopathology. These data suggest a central role for macrophages and IL-1 signaling in the inflammatory process triggered by ricin.”

The full article can be found at: (M.L. Lindauer, et. al., “Pulmonary Inflammation Triggered by Ricin Toxin Requires Macrophages and IL-1 Signaling”. *Journal of Immunology*, 2009; 183 (2):1419-1426). Link not available.

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