

13 May 2010

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

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Chem-Bio News - S&T Edition

- 1. CDC HEALTH ADVISORY - POTENTIAL FOR Q FEVER INFECTION AMONG TRAVELERS RETURNING FROM IRAQ AND THE NETHERLANDS:** *"Increasing reports of Q fever among deployed U.S. military personnel due to endemic transmission in Iraq, as well as a large ongoing outbreak of Q fever in the Netherlands, may place travelers to these regions at risk for infection."*
- 2. PHARMACOKINETIC-PHARMACODYNAMIC ASSESSMENT OF FAROPENEM IN A LETHAL MURINE BACILLUS ANTHRACIS INHALATION POSTEXPOSURE PROPHYLAXIS MODEL:** *"Overall, faropenem demonstrated a high level of activity against B. anthracis in the murine postexposure prophylaxis inhalation model."*
- 3. SINGLE LABORATORY VALIDATION OF A SURFACE PLASMON RESONANCE BIOSENSOR SCREENING METHOD FOR PARALYTIC SHELLFISH POISONING TOXINS:** *"Natural samples were also evaluated and the resultant data displayed overall agreements of 96 and 92% with that of the existing AOAC approved methods of mouse bioassay (MBA) and high performance liquid chromatography (HPLC), respectively."*
- 4. PREPARATION AND CHARACTERISTICS OF ORIDONIN-LOADED NANOSTRUCTURED LIPID CARRIERS AS A CONTROLLED-RELEASE DELIVERY SYSTEM:** *"These results indicated that nanostructured lipid carriers could potentially be exploited as a delivery system with improved drug entrapment efficiency and controlled drug release."*
- 5. SURFACE FUNCTIONALIZATION OF POLYKETAL MICROPARTICLES WITH NITRILOTRIACETIC ACID-NICKEL COMPLEXES FOR EFFICIENT PROTEIN CAPTURE AND DELIVERY:** *"In summary, we show that immobilized metal affinity strategies have the potential to improve targeting and protein delivery via degradable polymer microparticles."*
- 6. DEVELOPMENT OF A NOVEL IMMUNO-PCR ASSAY FOR DETECTION OF RICIN IN GROUND BEEF, LIQUID CHICKEN EGG, AND MILK:** *"Among the four formats investigated, the pAb-pAb combination yielded the lowest limit of detection (10 fg/ml)."*
- 7. METALLOTHIONEIN-I/II CARDIOMYOCYTES ARE SENSITIVE TO FUSARIUM MYCOTOXIN BUTENOLIDE-INDUCED CYTOTOXICITY AND OXIDATIVE DNA DAMAGE:** *"Taken together, these findings clearly show that basal MT [metallothionein] can efficiently attenuate BUT [butenolide]-induced cytotoxic injuries in cardiomyocytes via the inhibition of intracellular ROS production, and associated DNA damage."*
- 8. MICROORGANISMS IN TOXIC GROUNDWATER FINE-TUNED TO SURVIVE:** *"The metagenomic study of a "stressed" microbial community in groundwater near a former waste disposal pond site on DOE's Oak Ridge Reservation (ORR) revealed microbes with an overabundance of genes involved in DNA recombination and repair and other defense mechanisms for dealing with contaminants and other environmental stresses."*
- 9. ORNL [OAK RIDGE NATIONAL LABORATORY] TECHNOLOGY RAISES BAR, LOWERS COST FOR GROUNDWATER CONTAMINANT SENSORS:** *"The proprietary system, called membrane-extraction ion mobility spectrometry, is a single compact device able to detect aqueous tetrachloroethylene and trichloroethylene concentrations as low as 75 micrograms per liter with a monitoring duty cycle of three minutes. Xu noted that this technology would reduce the cost of long-term monitoring of contaminants in groundwater by up to 80 percent..... Also, additional membranes with different properties can be installed to enable collection of a wider variety of contaminants."*
- 10. rhEGF MICROSPPHERE FORMULATION AND IN VITRO SKIN EVALUATION:** *"Therefore, rhEGF-PCL microparticles seemed to be promising systems due to their ability to provide locally a sustained release of rhEGF in skin layers."*

CB Daily Report

Chem-Bio News

CDC HEALTH ADVISORY - POTENTIAL FOR Q FEVER INFECTION AMONG TRAVELERS RETURNING FROM IRAQ AND THE NETHERLANDS

US Centers for Disease Control and Prevention
May 12, 2010

“THIS IS AN OFFICIAL CDC HEALTH ADVISORY

Distributed via Health Alert Network
Wednesday, May 12, 2010, 16:35 EST (4:35 PM EST)
CDCHAN-00313-2010-05-12-ADV-N

Potential for Q Fever Infection Among Travelers Returning from Iraq and the Netherlands

Summary

Increasing reports of Q fever among deployed U.S. military personnel due to endemic transmission in Iraq, as well as a large ongoing outbreak of Q fever in the Netherlands, may place travelers to these regions at risk for infection. Healthcare providers in the United States should consider Q fever in the differential diagnosis of persons with febrile illness, pneumonia or hepatitis who have recently been in Iraq or the Netherlands. Physicians are encouraged to submit samples for proper laboratory testing and contact the CDC for consultation if needed. Q fever cases in travelers should be promptly reported to proper authorities.”

The full article can be found at: <http://www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00313>
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PHARMACOKINETIC-PHARMACODYNAMIC ASSESSMENT OF FAROPENEM IN A LETHAL MURINE BACILLUS ANTHRACIS INHALATION POSTEXPOSURE PROPHYLAXIS MODEL

Drug Week
May 7, 2010

“There are few options for prophylaxis after exposure to Bacillus anthracis, especially in children and women of childbearing potential. Faropenem is a beta-lactam in the penem subclass that is being developed as an oral prodrug, faropenem medoxomil, for the treatment of respiratory tract infections.”

“Faropenem was shown to have in vitro activity against B. anthracis strains that variably express the bla₁ beta-lactamase (MIC range, ≤ 0.06 to 1 microg/ml). In this study we evaluated the pharmacokinetic-pharmacodynamic (PK-PD) relationships between the plasma faropenem free-drug (f) concentrations and efficacy against B. anthracis in a murine postexposure prophylaxis inhalation model. The plasma PKs and PKs-PDs of faropenem were evaluated in BALB/c mice following the intraperitoneal (i.p.) administration of doses ranging from 2.5 to 160 mg/kg of body weight. For the evaluation of efficacy, mice received by inhalation aerosol doses of B. anthracis (Ames strain; faropenem MIC, 0.06 microg/ml) at 100 times the 50% lethal dose. The faropenem dosing regimens (10, 20, 40, and 80 mg/kg/day) were administered i.p. at 24 h postchallenge at 4-, 6-, and 12-h intervals for 14 days. The sigmoid maximum-threshold-of-efficacy (E(max)) model fit the survival data, in which the free-drug area under the concentration-time curve (fAUC)/MIC ratio, the maximum concentration of free drug in plasma (fC(max))/MIC ratio, and the cumulative percentage of a 24-h period that the free-drug concentration exceeds the MIC under steady-state pharmacokinetic conditions (f %T(MIC)) were each evaluated. Assessment of f %T(MIC) demonstrated the strongest correlation with survival (R(2)=0.967) compared

to the correlations achieved by assessment of fAUC/MIC or fC(max)/MIC, for which minimal correlations were observed. The 50% effective dose (ED(50)), ED(90), and ED(99) corresponded to f %T(MIC) values of 10.6, 13.4, and 16.4%, respectively, and E(max) was 89.3%."

"Overall, faropenem demonstrated a high level of activity against B. anthracis in the murine postexposure prophylaxis inhalation model."

The full article can be found at: (S.C. Gill, et. al., "Pharmacokinetic-pharmacodynamic assessment of faropenem in a lethal murine Bacillus anthracis inhalation postexposure prophylaxis model". Antimicrobial Agents and Chemotherapy, 2010;54(5):1678-83). Link not available.

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SINGLE LABORATORY VALIDATION OF A SURFACE PLASMON RESONANCE BIOSENSOR SCREENING METHOD FOR PARALYTIC SHELLFISH POISONING TOXINS

Life Science Weekly

May 4, 2010

"A research element of the European Union (EU) sixth Framework project BioCop focused on the development of a surface plasmon resonance (SPR) biosensor assay for the detection of paralytic shellfish poisoning (PSP) toxins in shellfish as an alternative to the increasingly ethically unacceptable mouse bioassay. A biosensor assay was developed using both a saxitoxin binding protein and chip surface in tandem with a highly efficient simple extraction procedure."

"The present report describes the single laboratory validation of this immunological screening method, for this complex group of toxins with differing toxicities, according to the European Decision 2002/657/EC in conjunction with IUPAC and AOAC single laboratory validation guidelines. The different performance characteristics (detection capability CC beta, specificity/selectivity, repeatability, reproducibility, stability, and applicability) were determined in relation to the EU regulatory limit of 800 mu g of saxitoxin equivalents (STX eq) per kg of shellfish meat. The detection capability CC beta was calculated to be 120 mu g/kg. Intra-assay repeatability was found to be between 2.5 and 12.3% and interassay reproducibility was between 6.1 and 15.2% for different shellfish matrices."

"Natural samples were also evaluated and the resultant data displayed overall agreements of 96 and 92% with that of the existing AOAC approved methods of mouse bioassay (MBA) and high performance liquid chromatography (HPLC), respectively."

The full article can be found at: (K. Campbell, et. al., "Single Laboratory Validation of a Surface Plasmon Resonance Biosensor Screening method for Paralytic Shellfish Poisoning Toxins". Analytical Chemistry, 2010;82(7):2977-2988). Link not available.

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PREPARATION AND CHARACTERISTICS OF ORIDONIN-LOADED NANOSTRUCTURED LIPID CARRIERS AS A CONTROLLED-RELEASE DELIVERY SYSTEM

Life Science Weekly

May 11, 2010

"In order to improve drug entrapment efficiency and loading capacity, nanostructured lipid carriers consisting of solid lipid and liquid lipid as a new type of colloidal drug delivery system were prepared. The dispersions of oridonin-loaded solid lipid nanoparticles and nanostructured lipid carriers were successfully prepared by the emulsion-evaporation and low temperature-solidification technique using monostearin as the solid lipid, caprylic/capric triglycerides as the liquid lipid and oridonin as the model drug."

"Their physicochemical properties of oridonin-loaded nanostructured lipid carriers and release behaviours were investigated and compared with those of solid lipid nanoparticles. As a result, the mean particle size was approximately 200 nm with narrow polydispersity index lower than 0.4 for all

developed formulations. Zeta potential values were in the range -35 mV approximately -50 mV, providing good physical stability of all formulations. The differential scanning calorimetry and X-ray diffraction analysis results demonstrated lipid nanoparticles exhibited crystal order disturbance and thus left more space to accommodate drug molecules. The improved drug entrapment efficiency and loading capacity were observed for nanostructured lipid carriers and they enhanced with increasing the caprylic/capric triglycerides content. In vitro drug release experiments exhibited biphasic drug release patterns with burst release initially and prolonged release afterwards."

"These results indicated that nanostructured lipid carriers could potentially be exploited as a delivery system with improved drug entrapment efficiency and controlled drug release."

The full article can be found at: (W. Dai, et. al., "Preparation and characteristics of oridonin-loaded nanostructured lipid carriers as a controlled-release delivery system". Journal of Microencapsulation, 2010;27(3):234-41). Link not available.

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SURFACE FUNCTIONALIZATION OF POLYKETAL MICROPARTICLES WITH NITRILOTRIACETIC ACID-NICKEL COMPLEXES FOR EFFICIENT PROTEIN CAPTURE AND DELIVERY

Drug Week

May 7, 2010

"In this work, we have adapted a widely used immobilized metal affinity protein purification strategy to non-covalently attach proteins to the surface of microparticles. Polyketal microparticles were surface modified with nitrilotriacetic acid-nickel complexes which have a high affinity for sequential histidine tags on proteins. We demonstrate that this high affinity interaction can efficiently capture proteins from dilute solutions with little risk of protein denaturation. Proteins that bound to the Ni-NTA complex retain activity and can diffuse away from the microparticles to activate cells from a distance. In addition, this surface modification can also be used for microparticle targeting by tethering cell-specific ligands to the surface of the particles, using VE-Cadherin and endothelial cells as a model."

In summary, we show that immobilized metal affinity strategies have the potential to improve targeting and protein delivery via degradable polymer microparticles."

The full article can be found at: (J.C. Sy, et. al., "Surface functionalization of polyketal microparticles with nitrilotriacetic acid-nickel complexes for efficient protein capture and delivery". Biomaterials, 2010;31(18):4987-94). Link not available.

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DEVELOPMENT OF A NOVEL IMMUNO-PCR ASSAY FOR DETECTION OF RICIN IN GROUND BEEF, LIQUID CHICKEN EGG, AND MILK

Food & Farm Week

May 13, 2010

"In this study, we developed procedures for quantification of ricin in foods using immuno-PCR (IPCR). The direct adsorption of ricin onto the wells of a microtitration plate was compared with indirect immobilization via a capture antibody (sandwich IPCR). The latter procedure provided much greater sensitivity. We also compared a protocol with the immunoassay and PCR conducted in a single plate to a two-step procedure in which the PCR was conducted in a second plate, following release and transfer of the DNA marker. The two-step procedure proved 1,000-fold more sensitive for ricin detection, so this format was used to detect ricin in spiked samples of ground beef, chicken egg, and milk, and the results were compared with those obtained from enzyme-linked immunosorbent assay (ELISA). The IPCR had a limit of detection of 10 pg/ml in chicken egg and milk samples and 100 pg/ml in ground beef extracts. Comparable ELISA results were in the 1 to 10 ng/ml range. Thus, IPCR affords sensitivity that is 10-fold greater in the ground beef matrix, 100-fold greater in the milk, and 1,000-fold greater in the egg matrix than the sensitivity obtained by ELISA. Further optimization of the sandwich IPCR was performed by comparing various antibody combinations."

"Among the four formats investigated, the pAb-pAb combination yielded the lowest limit of detection (10 fg/ml)."

The full article can be found at: (X.H. He, et. al., "Development of a Novel Immuno-PCR Assay for Detection of Ricin in Ground Beef, Liquid Chicken Egg, and Milk". Journal of Food Protection, 2010;73(4):695-700). Link not available.

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METALLOTHIONEIN-I/II CARDIOMYOCYTES ARE SENSITIVE TO FUSARIUM MYCOTOXIN BUTENOLIDE-INDUCED CYTOTOXICITY AND OXIDATIVE DNA DAMAGE

Biotech Week

May 5, 2010

"Previous studies revealed butenolide (BUT), a Fusarium mycotoxin distributes extensively, induced myocardial oxidative damage, which could be abated by antioxidants such as glutathione. Metallothionein (MT) has proved to attenuate several oxidative cardiomyopathies via its potent antioxidant property."

"The present study is therefore undertaken to investigate the protective potential of the endogenous expression of MT against BUT-induced myocardial toxicity. Primary cultures of neonatal cardiomyocytes from MT-I/II mice along with the corresponding wild-type mice will be utilized to determine the possible mechanistic properties of MT. BUT treatment to the cardiomyocytes evoked significant cytotoxicity as evidenced by morphological changes and concentration- and time-dependent reductions in cell viability. Additionally, BUT treatment remarkably increased reactive oxygen species (ROS) production in the cardiomyocytes of both MT-I/II and wild-type mice. As a result, noticeable DNA damage in both cardiomyocytes was detected by alkaline comet assay. Furthermore, the comparison between the MT-I/II and wild-type cardiomyocytes indicated that ROS production in the cardiomyocytes from the MT-I/II mice was higher than from wild-type mice. DNA damage as evaluated by percentage of comet tail DNA, tail length and tail moment was more severe in the MT-I/II cardiomyocytes than in wild-type myocytes. And in agreement with those results mentioned above, the MT-I/II cardiomyocytes were more sensitive to BUT-induced cytotoxicity than wild-type cardiomyocytes."

"Taken together, these findings clearly show that basal MT can efficiently attenuate BUT-induced cytotoxic injuries in cardiomyocytes via the inhibition of intracellular ROS production, and associated DNA damage."

The full article can be found at: (H.Y. Yang, et. al., "Metallothionein-I/II cardiomyocytes are sensitive to Fusarium mycotoxin butenolide-induced cytotoxicity and oxidative DNA damage". Toxicon, 2010;55(7):1291-6). Link not available.

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MICROORGANISMS IN TOXIC GROUNDWATER FINE-TUNED TO SURVIVE

By Bill Cabage

Oak Ridge National Laboratory News Release

March 29, 2010

"Microorganisms can indeed live in extreme environments, but the ones that do are highly adapted to survive and little else, according to a collaboration that includes Department of Energy's Oak Ridge National Laboratory and Joint Genome Institute (JGI) and the University of Oklahoma.

The metagenomic study of a "stressed" microbial community in groundwater near a former waste

disposal pond site on DOE's Oak Ridge Reservation (ORR) revealed microbes with an overabundance of genes involved in DNA recombination and repair and other defense mechanisms for dealing with contaminants and other environmental stresses.

The studies, said ORNL researcher David Watson, are ultimately aimed at developing biologically based methods for reducing the level of the contaminants in the groundwater, which at the ORR site includes nitrates, solvents and heavy metals, including uranium."

The full article can be found at: http://www.ornl.gov/info/press_releases/get_press_release.cfm?ReleaseNumber=mr20100329-00

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ORNL [OAK RIDGE NATIONAL LABORATORY] TECHNOLOGY RAISES BAR, LOWERS COST FOR GROUNDWATER CONTAMINANT SENSORS

By Ron Walli

Oak Ridge National Laboratory News Release

May 06, 2010

"While laboratory-based technologies for analysis of water contaminants are time-consuming, labor-intensive and expensive, the method introduced in a paper published in *Analytical Chemistry* is eloquent. The system combines a membrane tube and an ion mobility analysis system, or analyzer, creating a single procedure for in-situ monitoring of chlorinated hydrocarbons in water.

"Our technology represents a low-cost yet highly accurate way to monitor contaminants in water and air," said Chemical Sciences Division researcher Jun Xu, the lead researcher for the project.

The proprietary system, called membrane-extraction ion mobility spectrometry, is a single compact device able to detect aqueous tetrachloroethylene and trichloroethylene concentrations as low as 75 micrograms per liter with a monitoring duty cycle of three minutes. Xu noted that this technology would reduce the cost of long-term monitoring of contaminants in groundwater by up to 80 percent."

.....

"Groundwater monitoring, however, is just one example of the technology's capabilities. The sensor can also be configured to monitor well, tap or river water or other water suspected of having an undesirable or possibly illegal level of contamination. Also, additional membranes with different properties can be installed to enable collection of a wider variety of contaminants.

Co-authors of the paper, titled "Membrane-extraction ion mobility spectrometry for in situ detection of chlorinated hydrocarbons in water," are Yongzhai Du, Wei Zhang, William Whitten and David Watson of ORNL and Haiyang Li of the Dalian Institute of Chemical Physics, Chinese Academy of Science."

The full article can be found at: http://www.ornl.gov/info/press_releases/get_press_release.cfm?ReleaseNumber=mr20100506-00

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rhEGF MICROSPHERE FORMULATION AND IN VITRO SKIN EVALUATION

Biotech Week

May 5, 2010

"An optimized process for protein encapsulation was applied to formulate epidermal growth factor (rhEGF)-poly-epsilon-caprolactone microspheres. Microparticles mean size was 3.8 μm +/- 0.2 and the encapsulation efficiency was 41.9% +/- 2.6. rhEGF recovery after the encapsulation process was similar to 70% (41.9% inside the microspheres and 30% still active in the external phase)."

"In vitro release experiments in McIlvaine buffered solution showed a rhEGF sustained release over 4 days. Skin absorption studies conducted on full-thickness human skin using the Franz cell method showed that 20% rhEGF was released from the microspheres after 24 h exposure. Microspheres accumulated in the stratum corneum where they may act as a rhEGF reservoir."

"Therefore, rhEGF-PCL microparticles seemed to be promising systems due to their ability to provide locally a sustained release of rhEGF in skin layers."

The full article can be found at: (L. Alhaushey, et. al., "rhEGF microsphere formulation and in vitro skin evaluation". Journal of Microencapsulation, 2010;27(1):14-24). Link not available.

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