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Conventional analytical methods for chemical warfare agents*

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Abstract: Analytical methods that are currently used for the detection and identification of chemical warfare agents are reviewed and classified by the number of dimensions of information they provide. Single-dimensional sensors target specific compounds or classes of compounds. Although they can be less expensive and more portable than multidimensional sensors, multidimensional sensors detect a broader threat spectrum with greater precision and accuracy. The recommendation for analytical field verification during inspections under the Chemical Weapons Convention (CWC) is to use simple two-dimensional analytical methods, such as gas chromatography (GC) or ion mobility spectrometry (IMS), for on-site screening of chemical weapons (CW) agents or to fully equip a modern, mobile analytical laboratory located in an airplane, which can be moved rapidly throughout the world to each inspection site and provide high-quality analytical data on-site.

INTRODUCTION

> "The inspection team shall have the right to perform on-site analysis of samples using approved equipment brought by it." [Verification Annex, Part II.E.53 of the Chemical Weapons Convention of 1993.]

Although the CWC of 1993 calls for the on-site verification of chemical warfare agents by analytical methods, no such verifications are performed. Yet, verification is needed to insure that chemical weapons are not present or that agents being destroyed have been identified correctly. Only paper records and declarations have been used to verify the presence or absence of chemical warfare agents [1].

So, why aren't routine analyses of chemical weapons performed during the inspection process? Perhaps it depends on what the definition of "shall" shall be. Interpretation of the intent of the CWC can lead to the conclusion that analytical verification is not a requirement. Certainly, the cost of multiple and complex analyses can quickly become prohibitive. However, the primary reason that analyses are not performed on a routine basis is the lack of "approved equipment" that can conveniently be transported to the test site [1]. To date, the only "approved equipment" for field verification of chemical warfare agents is a gas chromatograph coupled with a mass spectrometer (GC/MS). While GC/MS is one of the most powerful analytical instruments available, it is also one of the most complex and difficult to maintain and operate on a routine basis.

Another problem, in addition to complex analytical instrumentation, is that the biological and chemical warfare agent threat spectrum is broad, ranging from relatively simple chemical agents to

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complex bioengineered microorganisms. Traditional chemical agents—nerve, vesicant, and blood agents—have acute toxicities in the range of 10^{-3} g/person and are relatively easy to detect. Emerging chemical agents (toxic chemicals and aerosols) and bioregulators (neuropeptides and psychoactive compounds) are more varied in their chemical structure, requiring more sophisticated analytical methods for identification and detection. The most difficult chemical agents to detect are the cytotoxins and neurotoxins with chronic toxicities as low as 10^{-10} g/person [2].

To identify and detect this complex array of chemicals, the ideal instrument would respond within 5 min, cover the 15 to 200 000 dalton threat spectrum, have high sensitivity and reproducibility, exhibit enough resolving power to specifically respond to each chemical agent, necessitate little or no sample preparation, consume a minimal amount of analytical reagents, and be suitable for field operation. In short, it appears that what is required for CW verification is a "tricorder" [3]. A tricorder is a mythical hand-held analytical instrument developed for the production of a science fiction television show called *Star Trek*, which was first broadcast in the fall of 1966. Completely wireless, simply pointing the cassette-sized instrument at an object produced complete chemical analysis on its miniature screen within seconds. Unfortunately, the concept of such an ideal instrument has apparently altered our understanding of state-of-the-art analytical instrumentation to the point that nothing less than a tricorder-like instrument can be accepted as "approved equipment" for chemical warfare agent detection in the field.

For sure, a small hand-held, broad-spectrum device is desirable for all types of analytical applications, but is such an instrument possible? However, before we can determine where we want to go, we must understand where we are. In reality, there are only four approaches to analytical measurement of chemical warfare agents: (1) one-dimensional sensors, which rely on the selective detection of the analyte; (2) two-dimensional sensors, in which a separation step is coupled with selective detection; (3) three-dimensional sensors, in which a two-dimensional separation step is coupled with selective detection; and (4) four-dimensional sensors, in which a three-dimensional separation step is coupled with selective detection. The objective of this article is to review the state of the art of these sensors with respect to the detection and identification of chemical warfare agents.

ONE-DIMENSIONAL SENSORS (SELECTIVE DETECTORS)

The simplest approach for chemical detection is to target the specific compound of interest and selectively detect it in the presence of other background compounds and interferences.

Surface acoustic wave (SAW) sensors

One of the most popular approaches for selective sensing of CW agents is the SAW sensor. First reported by Wohltjen and Dessy in 1979 [4] and based on the GC piezoelectric response demonstrated by King in 1964 [5], this sensor detects adsorption of an analyte on the surface of a piezoelectric crystal. When a time-varying electric field is applied to one side of a piezoelectric material, it sets up an acoustic wave that is propagated along the surface of the piezoelectric material and detected by electrodes located at the other end of the material. Changes in amplitude or phase of this wave occur when an analyte adsorbs onto the surface of the piezoelectric material. When the surface is coated with a thin film, which adsorbs chemicals selectively, a selective sensor is produced. A general review of these types of sensors was published in 1997 [6].

Early work on the application of SAW instruments to CW agent detection reported the development of a temperature-controlled array of SAW devices with automated sample preconcentration and pattern recognition [7]. Detection limits as low as 0.01 mg/m^3 for organophosphorus analytes and 0.5 mg/m^3 for organosulfur analytes were obtained within 2 min. Besides the difficulty of developing selective coatings for SAW sensors, polymer films can dewet the surface and produce isolated droplets of material, leading to a degradation of response [8].

The major advantage of SAW detectors is that they can be made small and portable. The U.S. Military has developed a small sensor based on SAW technology called the joint chemical agent detector (JCAD). For 10-s monitoring time, the JCAD has a threshold detection level of 1 mg/m^3 for both V- and G-type nerve agents. Threshold detection levels for vesicant blister agents such as lewisite were found to be slightly higher at 50 mg/m^3. However, in 1 min, typical blood agents like AC or CK can be detected at 22 mg/m^3 and 20 mg/m^3, respectively [9].

The SAWRHINO is based on the SAW system and has been developed for vehicular mounted field applications. It is an automated chemical agent detector, providing reversible responses for G-nerve and H-mustard agents. The SAWRHINO is reported to provide 7 orders of magnitude from a detection limit of 200 parts per trillion [10].

Electrochemical sensors

Direct determination of organophosphate nerve agents can also be accomplished using the amperometric response of an enzyme biosensor [11,12]. In this approach, the biosensor incorporated the enzyme organophosphorus hydrolase by covalently immobilizing it on glass beads. The enzyme hydrolyzes organophosphate to an electroactive species, which can be determined amperometrically. Best results were achieved with organophosphates containing a nitrophenyl group. This approach has been incorporated into a single-channel microchip for the rapid screening of organophosphate nerve agents [13]. Chemiresistive vapor detectors for nerve agent simulants have also been reported [14]. They use a conducting polymer composite that changes electrical resistance when an agent adsorbs onto the surface. The detection limit for this sensor is in the range of 47–240 μg/m^3 of dimethyl methyl phosphonate (DMMP) in air.

Spectrophotometric sensors

The least expensive approach to chemical agent detection is the use of the color spot test. Chemical agent detector kits are available that can identify field concentrations of nerve agents (GB, GA, GC, GF, and VX), vesicant agents (mustard, phosgene oxime, mustard-lewisite, and lewisite), and blood agents (hydrogen cyanide and cyanogen chloride) in about 15–20 min. Chemical agents are adsorbed onto a pretreated test spot, and when a "developer" reagent is added, specific color changes indicate the presence or absence of chemical agents. The problem with the spot test approach is that it is too slow and insensitive for early warning detection and not sufficiently selective to provide reliable verification. Nevertheless, for CW verification, the spot test approach is a convenient method for initial screening.

More sophisticated color detection relies on the use of spectrophotometers. Techniques of molecular imprinting have been combined with sensitized lanthanide luminescence to create a selective sensor for nerve agents [15]. When hydrolysis products of a chemical warfare nerve agent such as sarin or soman adsorb to the imprinted polymer, a narrow luminescence band in the 610-nm region of the Eu^{3+} spectrum appears due to a shift in the ligand field. The limit of detection for this method is on the order of 7 ppt in solution with a linear range up to 10 ppm. Immobilized whole-cell photosynthetic microorganisms have been used for stand-off detection of airborne chemical warfare agents and simulants using well-known principles of fluorescence induction [16]. The fluorescence signal from the sensors is stable for up to 40 days.

Immunochemical sensors

Immunochemical sensors potentially offer a more specific alternative to the relatively nonspecific color reactions involved with spot tests. In this approach, a protein antibody is developed that binds specifically to the chemical agent and elicits some type of analytical response. Fluorescence and electrochemical responses have been used. However, enzyme-linked immunoabsorbent assays (ELISA) have

proven most useful for the detection of a variety of nerve agents. For example, soman, even in the presence of its major hydrolysis product, can be detected down to levels of 180 ng/ml (180 ppb) [17]. A major problem with immunochemical sensors is that they are slow, taking up to 2 h in some cases. While this is a problem for early warning of a chemical attack, specific ELISA sensors could be used for verification. In general, immunochemical assays are expensive to develop, but can be inexpensive for large numbers of assays. Another problem for field analysis is the stability of the antibody in a variety of environmental conditions and for long periods of time. For these reasons, immunochemical assays have not reached their potential as a simple, sensitive, and selective assay for chemical warfare agents.

TWO-DIMENSIONAL SENSORS

Due to the complex nature of the agents and their matrices, nonseparation-based analytical methods often experience interferences, which result in false positive or negative responses. Thus, some type of separation method is often coupled to an analytical detector to provide more specificity of response and a broader range of application. The most common separation devices are GC, liquid chromatography (LC), capillary electrophoresis (CE), IMS, and mass spectrometry (MS). A brief description of each method along with recent research in the area of CW agent detection is given below.

Gas chromatography (GC)

For vapor-phase chemical warfare agents, GC is usually the analytical separation method of choice. In general, a high-resolution gas chromatographic separation can require up to 30 min for complete separation and detection of a complex mixture. However, when selective detectors are used in combination with GC, the separation time can be reduced significantly. For example, using a pulsed-flame photometric detector, which is highly selective for phosphorus- and sulfur-containing compounds, detection of 20 ng/m^3 of organophosphorus compounds and 200 ng/m^3 for organosulfur compounds can be accomplished within 30 s [18].

Collection and concentration in tubes packed with selected adsorbents followed by thermal desorption of the agent and gas chromatographic separation proved to be useful for both high- and low-volatility analytes [19]. Collection and concentration are also convenient for GC using solid-phase microextraction (SPME) methods. Selective SPME prior to sample introduction into a GC increases the selectivity of the analysis for sarin [20]. Sulfur mustard has also been detected by SPME in soil samples [21].

Liquid chromatography (LC)

For compounds that are not volatile or thermally labile, LC rather than GC is often the method of choice for separation prior to detection. However, high pressures and small particle sizes limit column length and, therefore, the ultimate resolving power possible by LC. In addition, low diffusion rates in liquids make LC a relatively slow analytical method for the detection of CW agents.

Nevertheless, a number of applications have been reported. For example, hydrolysis products of sulfur mustards can be determined at the ppm level in about 20 min per sample by reversed-phase liquid chromatography (RPLC) coupled with a sulfur flame photometric detector [22]. Similarly, aqueous samples of alkylphosphonic acids can be analyzed at the ppt level in about 20 min/sample by reversed-phase LC coupled with phosphorous selective flame photometric detection [23].

Capillary electrophoresis (CE)

For higher resolving power than is possible with RPLC (or faster analysis times with similar resolving power), CE is the separation method of choice for ionic and ionizable compounds. Coupled with selective detectors such as the flame photometric detector, CE can detect alkylphosphonic acids in water at the 0.1–0.5 μg/ml level in less than 10 min [24]. Indirect UV absorbance detection has also been reported for the detection of these compounds after CE [25]. The use of electrokinetic injection improved detection limits for a number of degradation products. For example, methylphosphonic acid (MPA), ethylmethylphosphonic acid (EMPA), isopropylmethylphosphonic acid (IMPA), and pinacolylmethylphosphonic acid (PMPA) were detected at the ppb level in 3 min from water samples [26].

A miniaturized analytical system has been reported for the separation and detection of nerve agents using CE microchips with amperometric detection [27].

Ion mobility spectrometry (IMS)

IMS is a separation method in which gas-phase ions, created by the vapor-phase ionization of neutral molecules using photon-, corona- or radioactive ionization processes (or by the liquid-phase ionization of both neutral, ionic, and ionizable molecules using electrospray or coronospray ionization processes), are separated according to their differences in velocities through a gas in an electric field. In IMS, ions separate according to their size-to-charge ratio.

Ion mobility instruments that have been used for the field detection of CW agents are the chemical agent monitor (CAM) and the improved chemical agent monitor (ICAM). Using a radioactive ionization source, they require only 1 min of exposure time to detect vapors of H-type vesicant agents as well as G- and V-type nerve agents. In addition to the CAM and ICAM, the automatic chemical agent detection alarm (ACADA) is also based on IMS technology. Used as a man-portable and point-sampling alarm system, the ACADA provides concurrent nerve and vesicant agent detection at improved sensitivity.

To date, all ion mobility measurements made for CW agents have been direct mobility measurements made under low electric field conditions in which the ion mobility is directly proportional to the electric field strength. However, a new and promising method for using ion mobility for monitoring gas-phase ions takes advantage of the nonlinear behavior of ion mobilities under high electric field strength conditions [28]. Unfortunately, the resolving power of this novel approach is currently too low to provide adequate selectivity for CW agent detection, but the absence of an ion gate promises improved sensitivity over traditional IMS instruments.

A third type of IMS that is used for the detection of CW agents is called aspiration IMS [29]. In this system, the ions travel through an orthogonal electric field in which the ions are deflected to multichannels located on the collecting electrode. Ions with higher mobilities are deflected to electrodes faster than ions with lower mobilities. Although these types of detectors also suffer from low resolving power, they also have the advantage of not requiring an ion gate. They have been applied to the detection of soman and VX degradation products.

Mass spectrometry (MS)

Unlike IMS, MS is an ion separation method in which gas-phase ions separate according to their mass to charge ratio as they move through a vacuum. Due to the lack of ion–molecule interactions and the rapid analysis time (on the order of μs), typical mass spectrometers have resolving powers 1 to 2 orders of magnitude better than IMS and chromatographic instruments. However, the complexity of requiring a vacuum limits the practical application of MS as a field analytical technique.

An ion trap mass spectrometer with a high-pressure negative ion source and selected reactant negative ions has been used to insure unambiguous detection of phosphorus- and nitrogen-containing

chemical warfare agents [30,31]. Ion traps can also be used for the direct determination of VX- and nitrogen-containing vesicant agents on the surface of soils at the ppm level using secondary ionization MS [32,33].

Matrix-assisted laser desorption ionization with time-of-flight mass spectrometry (MALDI-TOFMS) has been used for the determination of sulfur mustard exposure. When hemoglobin and metallothioneine are exposed to sulfur mustard, alkylation and cross-linking occurs [34].

Over the years, there have been a number of attempts to miniaturize the mass spectrometer. Recent approaches have been reported for the miniaturization of a time-of-flight mass spectrometers; one with an electron impact ionization source [35] and another with a photoionization ion source for the detection of phosphonates at the 10–100 ppb level [36]. Miniaturization of ion traps using a cylindrical design produced a detection limit for methyl salicylate of 1 pg with a resolution of 100 [37,38]. Ion trap MS has also been reported for the detection and identification of both chemical and biological agents in the field [39]. With this design, detection was based on respirable particle collection followed by liberation of derivatized biomarkers into the mass spectrometer.

MS, however, usually requires an additional separation step prior to the introduction of the sample into the spectrometry. This additional separation step serves to both kept the MS clean and to reduce the number of interferences in the ionization process or in the mass separational.

THREE-DIMENSIONAL SENSORS

Even with high-resolution, two-dimensional sensors, mistakes can be made with respect to identification of unknown analytes. Thus, for absolute identification, data obtained using three-dimensional sensors are normally recommended. Because of the complexity of these instruments, they are difficult to operate in the field without the support of a full mobile laboratory.

Gas chromatography/mass spectrometry (GC/MS)

GC/MS is the only analytical method of analysis that has been approved for chemical warfare verification, but due to the complex nature of this instrument, it has not been employed for field verification of chemical agents. However, GC/MS can provide some of the most reliable analytical information. An excellent and thorough review of the combination of chromatography with mass for CW agent determination has been conducted [40]. Currently, laboratory protocols for the GC/MS analyses of hydrolysis products of chemical warfare agents are available [41]. A recent discussion of the problems and possibilities associated with field-portable GC/MS has been reported based on environmental and forensic applications [42]. Also, a field-portable, high-speed GC/TOFMS has been reported [43].

Liquid chromatography/mass spectrometry (LC/MS)

In addition to GC/MS, LC is often employed to identify an unknown sample of chemical warfare agents [44]. Degradation products of CW agents are particularly difficult to determine due their lack of volatility for gas chromatographic separation and lack of chromophores for detection. Several ionization methods after liquid chromatographic separation have been found to be useful for the determination of CW degradation products. These ionization methods include particle beam ionization (PBI), electrospray ionization (ESI), and atmospheric pressure chemical ionization (APCI) [45]. Each ionization method was found to provide complementary information. But it has been the introduction of ESI that has enabled the most successful applications of LC methods coupled with MS. Thus, the determination of sarin, soman, and their hydrolysis products is now possible at the 10 μg/g level with liquid chromatographic separation followed by mass separation and detection [46].

Ion mobility/mass spectrometry (IM/MS)

As with MS, the development of ESI has enabled the introduction of nonvolatile compounds into the IMS. Using the IMS as a preseparation device, IMS serves as a rapid replacement for LC prior to the introduction into a mass spectrometer. CW degradation products have been separated and detected from water samples by using an IMS coupled to a quadrupole mass spectrometer (QMS) [47]. Not only do IMS separations have a greater resolving power than LC separations, they are also faster. Complete ion mobility spectra can be obtained within 20 ms. Even when several spectra are averaged to improve signal-to-noise ratio, separations occur in less than 10 s compared with 10–30 min for LC. With IMS/QMS separation and detection, the IMS is scanned continuously while the QMS is scanned slowly to produce the mobility-mass spectrum in about 10 min. Recently, however, IMS has been interfaced to a time-of-flight mass spectrometer, and complete mobility-mass spectra can be obtained in a few seconds [48]. In both IM/MS instruments, the detection limit for the CW degradation products is similar at about 100 ppb. The primary advantage of adding an IMS to the front of a mass spectrometer is to keep the mass spectrometer clean and to reduce the noise from that electrospray process in the mass spectrum. IM/MS data can also be collected for volatile CW simulants using a ^{63}Ni ionization source or a secondary ESI source.

Other three-dimensional sensors

Other three-dimensional analytical devices have been reported, although not specifically applied to CW agents. CE/MS can be interfaced similarly as LC, except that the high voltage at the end of the capillary column requires special approaches to isolate the voltage and assure proper potential on the electrospray needle. Thus, CE/MS has not found widespread use due to the complexity of its interface design. GC/GC utilizes a rapid switching technique to collect and inject a GC peak from a first high-resolution separation into a second fast chromatograph with a stationary phase of a different polarity from that of the first column. This approach supplies added information that can be used for qualitative analysis. LC/GC is also possible but has limited use due to the fact that compounds separated by LC are normally not amenable to gas chromatographic separation.

FOUR- AND MORE-DIMENSIONAL SENSORS

Given that chromatographic separations occur on the order of minutes, ion mobility separations on the order of milliseconds, and mass separations on the order of microseconds, four-dimensional sensors are possible when these separation techniques are coupled in series. Moreover, with some mass spectrometers it is possible to obtain MS/MS spectra or even MS^n spectra. Thus, it might be possible to have more than four-dimensional sensors such as GC/IMS/MS/MS/MS. Increasing the dimensional space in which a compound identification is determined decreases the possibility of false responses, although it does increase the complexity of the sensor.

CONCLUSIONS

So, is the development of a "tricorder"-like analytical instrument possible for use in verification of the CWC? Unfortunately, such a complex instrument is not achievable in the near future. The detection of targeted compounds does seem to be possible with relatively simple instrumentation, however, broad-spectrum analysis is more difficult. Nevertheless, lab-on-a-chip technology is being developed rapidly and the resolving power/instrument size ratio is increasing each year. Someday, perhaps the dream of a tricorder will not be so absurd as it appears today. Until then, how do we approach the problem of verifying the presence or absence of chemical weapons in the field?

Two approaches seem reasonable. The first, and least expensive, is to use the one- and two-dimensional approaches outlined above to screen compounds in the field. For example, field-portable gas chromatographs are readily available and relatively easy (much easier than the approved GC/MS instrument) to operate under field conditions [49]. IMSs are also relatively reliable these days (they are now used for explosive detection in most airports). Thus, it should be possible to use a variety of simple analytical instruments to obtain on-site supporting data on the presence or absence of chemical weapons. The second and more expensive approach would be to convert an airplane into a verification laboratory with full capabilities of a trace analysis laboratory for the identification and quantification of CW agents and their degradation products in all types of samples [50]. This mobile laboratory could be flown anywhere in the world and located near the site under evaluation. Samples could then be taken and analyzed on (or near) site within a few hours. Whatever the final solution, it does seem possible, even with conventional analytical methods, to provide confirmatory analytical data for verification activities mandated through the CWC of 1993.

REFERENCES

1. IUPAC Workshop: Impact of Scientific Developments on the Chemical Weapons Convention, Bergen, Norway, 1–3 July 2002.
2. *Chemical and Biological Defense Program*, U.S. Department of Defense (2002).
3. J. Reeves-Stevens and G. Reeves-Stevens. *The Art of Star Trek*, Pocket Books, New York (1995).
4. H. Wohltjen and R. Dessy. "Surface acoustic wave probe for chemical analysis. I. Introduction and instrument description", *Anal. Chem.* **51**, 1458–1464 (1979).
5. W. H. King, Jr. "Piezoelectric sorption detector", *Anal. Chem.* **36**, 1735–1739 (1964).
6. D. J. Ballantine, Jr., S. J. Martin, A. J. Ricco, G. C. Frye, E. T. Zellers, R. M. White, H. Wohltjen. *Acoustic Wave Sensors: Theory, Design and Physico-Chemical Applications*, Academic Press, San Diego (1996).
7. J. W. Grate, S. L. Rose-Pehrsson, D. L. Venezky, M. Klusty, H. Wohltjen. "Smart sensor system for trace organophosphorus and organosulfur vapor detection employing a temperature-controlled array of surface acoustic wave sensors, automated sample preconcentration, and pattern recognition", *Anal. Chem.* **65**, 1868–1881 (1993).
8. J. W. Grate and R. A. McGill. "Dewetting effects on polymer-coated surface acoustic wave vapor sensors", *Anal. Chem.* **67**, 4015–4019 (1995).
9. *Department of Defense Chemical and Biological Defense Program, Vol. 1: Annual Report to Congress,* U.S. Department of Defense (2002).
10. R. A. McGill, V. K. Nguyen, R. Chung, R. E. Shaffer, D. DiLella, J. L. Stepnowski, T. E. Mlsna, D. L. Venezky, D. Dominguez. "The 'NRLSAWRHINO': a nose for toxic gases", *Sens. Actuators B* **65**, 10–13 (2000).
11. A. Mulchandani, P. Mulchandani, W. Chen, J. Wang, L. Chen. "Amperometric thick-film strip electrodes for monitoring organophosphate nerve agents based on immobilized organophosphorus hydrolase", *Anal. Chem.* **71**, 2246–2249 (1999).
12. P. Mulchandani, W. Chen, A. Mulchandani. "Flow injection amperometric enzyme biosensor for direct determination of organophosphate nerve agents", *Environ. Sci. Technol.* **35**, 2562–2565 (2001).
13. J. Wang, M. Pumera, M. P. Chatrathi, A. Escarpa, M. Musameh, G. Collins, A. Mulchandani, Y. Lin, K. Olsen. "Single-channel microchip for fast screening and detailed identification of nitroaromatic explosives or organophosphate nerve agents", *Anal. Chem.* **74**, 1187–1191 (2002).

14. A. R. Hopkins and N. S. Lewis. "Detection and classification characteristics of arrays of carbon black/organic polymer composite chemiresistive vapor detectors for the nerve agent simulants dimethylmethylphosphonate and diisopropylmethylphosponate", *Anal. Chem.* **73**, 884–892 (2001).
15. A. L. Jenkins, O. M. Uy, G. M. Murray. "Polymer-based lanthanide luminescent sensor for detection of the hydrolysis product of the nerve agent Soman in water", *Anal. Chem*. **71**, 373–378 (1999).
16. C. A. Sanders, M. Rodriguez, Jr., E. Greenbaum. "Stand-off tissue-based biosensors for the detection of chemical warfare agents using photosynthetic fluorescence induction", *Biosens. Bioelectron.* **16**, 439–446 (2001).
17. D. E. Lenz, A. A. Brimfield, L. A. Cook. "Development of immunoassays for detection of chemical warfare agents", in *Immunochemical Technology for Environmental Applications*, D. A. Aga and E. M. Thurman (Eds.), pp. 77–86, ACS Symposium Series 657, American Chemical Society, Washington, DC (1997).
18. G. Frishman and A. Amirav. "Fast GC–PFPD system for field analysis of chemical warfare agents", *Field Anal. Chem. Technol.* **4**, 170–194 (2000).
19. W. A. Carrick, D. B. Cooper, B. Muir. "Retrospective identification of chemical warfare agents by high-temperature automatic thermal desorption-gas chromatography–mass spectrometry", *J. Chromatogr. A* **925**, 241–249 (2001).
20. S. D. Harvey, D. A. Nelson, B. W. Wright, J. W. Grate. Selective stationary phase for solid-phase microextraction analysis of sarin (GB). *J. Chromatogr. A* **954**, 217–225 (2002).
21. G. L. Kimm, G. L. Hook, P. A. Smith. "Application of headspace solid-phase microextraction and gas chromatography–mass spectrometry for detection of the chemical warfare agent bis(2-chloroethyl) sulfide in soil", *J. Chromatogr. A* **971**, 185–191, (2002).
22. E. W. J. Hooijschuur, C. E. Kientz, A. G. Hulst, U. A. Th. Brinkman. "Determination of hydrolysis products of sulfur mustards by reversed-phase microcolumn liquid chromatography coupled on-line with sulfur flame photometric detection and electrospray ionization mass spectrometry using large-volume injections and peak compression", *Anal. Chem.* **72**, 1199–1206 (2000).
23. E. W. J. Hooijschuur, C. E. Kientz, U. A. Th. Brinkman. "Determination of alkylphosphonic acids by microcolumn liquid chromatography with gradient elution coupled on-line with flame photometric detection", *J. Chromatogr. A* **907**, 165–172 (2001).
24. C. E. Kientz, E. W. J. Hooijschuur, U. A. Th. Brinkman. "Capillary electrophoresis coupled on-line with flame photometric detection: Determination of alkylphosphonic acids", *J. Micro. Sep.* **9**, 253–259 (1997).
25. J. E. Melanson, B. L.-Y. Wong, C. A. Boulet, C. A. Lucy. "High-sensitivity determination of the degradation products of chemical warfare agents by capillary electrophoresis-indirect UV absorbance detection", *J. Chromatogr. A* **920**, 359–365 (2001).
26. A.-E. F. Nassar, S. V. Lucas, L. D. Hoffland. "Determination of chemical warfare agent degradation products at low-part-per-billion levels in aqueous samples and sub-part-per-million levels in soils using capillary electrophoresis", *Anal. Chem.* **71**, 1285–1292 (1999).
27. J. Wang, M. P. Chatrathi, A. Mulchandani, W. Chen. "Capillary electrophoresis microchips for separation and detection of organophosphate nerve agents", *Anal. Chem.* **73**, 1804–1808 (2001).
28. R. A. Miller, E. G. Nazarov, G. A. Eiceman, A. T. King. "A MEMS radiofrequency ion mobility spectrometer for chemical vapor detection", *Sens. Actuators A* **91**, 301–312 (2001).
29. K. Tuovinen, H. Paakkanen, O. Hanninen. "Determination of soman and VX degradation products by an aspiration ion mobility spectrometry", *Anal. Chim. Acta* **440**, 151–159 (2001).

30. T. Faye, J. C. Mathurin, A. Brunot, J. C. Tabet, G. Wells, C. Fuche. "High-pressure ion source combined with an in-axis ion trap mass spectrometer. 2. Application of selective low-pressure negative ion chemical ionization", *Anal. Chem.* **72**, 5063–5069.
31. A. J. Bell, J. Murrell, C. M. Timperley, P. Watts. "Fragmentation and reactions of two isomeric O-alkyl S-(2-dialkylamino)ethyl methylphosphonothiolates studied by electrospray ionization/ion trap mass spectrometry", *J. Am. Soc. Mass Spectrom.* **12**, 902–910 (2001).
32. G. S. Groenewold, A. D. Appelhans, G. L. Gresham, J. E. Olson, M. Jeffery, J. B. Wright. "Analysis of VX on soil particles using ion trap secondary ion mass spectrometry", *Anal. Chem.* **71**, 2318–2323 (1999).
33. G. L. Gresham, G. S. Groenewold, J. E. Olson. "Identification of the nitrogen-based blister agents bis(2-chloroethyl)methylamine (HN-2) and tris(2-chloroethyl)amine (HN-3) and their hydrolysis products on soil using ion trap secondary ion mass spectrometry", *J. Mass Spectrom.* **35**, 1460–1469 (2000).
34. E. O. Price, J. R. Smith, C. R. Clark, J. J. Schlager, M. L. Shih. "MALDIToF/MS as a diagnostic tool for the confirmation of sulfur mustard exposure", *J. Appl. Toxicol.* **20**, S193–S197 (2000).
35. V. D. Berkout, R. J. Cotter, D. P. Segers. "Miniaturized EI/Q/oa TOF mass spectrometer", *J. Am. Soc. Mass Spectrom.* **12**, 641–647 (2001).
36. J. A. Syage, M. A. Hanning-Lee, K. A. Hanold. "A man-portable, photoionization time-of-flight mass spectrometer", *Field Anal. Chem. Technol.* **4**, 204–215 (2000).
37. G. E. Patterson, A. J. Guymon, L. S. Riter, M. Everly, J. Griep-Raming, B. C. Laughlin, Z. Ouyang, R. G. Cooks. "Miniature cylindrical ion trap mass spectrometer", *Anal. Chem*. **74**, 6145–6153 (2002).
38. L. S. Riter, Y. Peng, R. J. Noll, G. E. Patterson, T. Aggerholm, R. G. Cooks. "Analytical performance of a miniature cylindrical ion trap mass spectrometer", *Anal. Chem.* **74**, 6154–6162 (2002).
39. W. H. Griest, M. B. Wise, K. J. Hart, S. A. Lammert, C. V. Thompson. "Biological agent detection and indentification by the Block II Chemical Biological Mass Spectrometer", *Field Anal. Chem. Technol.* **5**, 177–184 (2001).
40. Ch. E. Kientz. "Chromatography and mass spectrometry of chemical warfare agents, toxins and related compounds: state of the art and future prospects", *J. Chromatogr. A* **814**, 1–23 (1998).
41. J. R. Smith, M. L. Shih, E. O. Price, G. E. Platoff, J. J. Schlager. "Army medical laboratory telemedicine: Role of mass spectrometry in telediagnosis for chemical and biological defense", *J. Appl. Toxicol.* **21**, S35–S41 (2001).
42. B. A. Eckenrode. "Environmental and forensic applications of field-portable GCMS: An overview", *J. Am. Soc. Mass. Spectrom.* **12**, 683–693 (2001).
43. J. A. Syage, B. J. Nies, M. D. Evans, K. A. Hanold. "Field-portable, high-speed GC/TOFMS", *J. Am. Soc. Mass Spectrom.* **12**, 648–655 (2001).
44. M. D. Brickhouse, W. R. Creasy, B. R. Williams, K. M. Morrissey, R. J. O'Connor, H. D. Durst. "Multiple-technique analytical characterization of a mixture containing chemical-weapons simulant from a munition", *J. Chromatogr. A* **883**, 185–198 (2000).
45. J. R. Smith and M. L. Shih. "Analysis of the degradation compounds of chemical warfare agents using liquid chromatography/mass spectrometry", *J. Appl. Toxicol.* **21**, S27–S34 (2001).
46. P. A. D'Agostino, J. R. Hancock, L. R. Provost. "Determination of sarin, soman and their hydrolysis products in soil by packed capillary liquid chromatography–electrospray mass spectrometry", *J. Chromatogr. A* **912**, 291–299 (2001).
47. G. R. Asbury, C. Wu, W. F. Siems, H. H. Hill, Jr. "Separation and identification of some chemical warfare degradation products using electrospray high resolution ion mobility spectrometry with mass selected detection", *Anal. Chim. Acta* **404**, 273–283 (2000).

48. W. E. Steiner, B. H. Clowers, L. M. Matz, W. F. Siems, H. H. Hill, Jr. "Rapid of aqueous chemical warfare agent degradation products: Ambient pressure ion mobility mass spectrometry", *Anal. Chem.* **74***,* 4343–4352 (2002).
49. C. M. Harris. "GC to go", *Anal. Chem.* **74**, 585A–589A (2002).
50. E. W. J. Hooijschuur, A. G. Hulst, A. L. deJong, L. P. de Reuver, S. H. van Krimpen, B. L. M. van Baar, E. R. J. Wils, C. E. Kientz, U. A. Th. Brinkman. "Identification of chemicals related to the chemical weapons convention during an interlaboratory proficiency test", *Trends Anal. Chem.* **21**, 116–130 (2002).