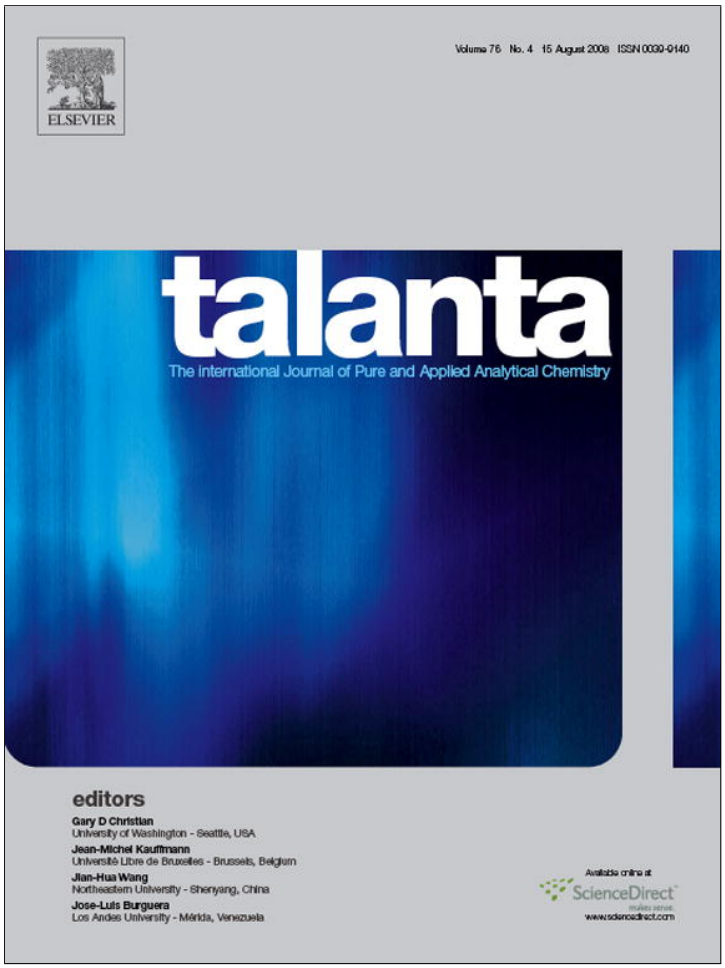

Talanta 76 (2008) 949–955

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Fabrication of polymer microsphere particle standards containing trace explosives using an oil/water emulsion solvent extraction piezoelectric printing process

Robert A. Fletcher[a,*], Jacquelyn A. Brazin[b], Matthew E. Staymates[a], Bruce A. Benner Jr.[a], J. Greg Gillen[a]

[a] National Institute of Standard and Technology, Gaithersburg, MD 20899, United States
[b] Massachusetts Institute of Technology, Cambridge, MA 02139, United States

ARTICLE INFO

Article history:
Received 6 February 2008
Received in revised form 24 April 2008
Accepted 25 April 2008
Available online 17 May 2008

Keywords:
Inkjet printing
Polymer particles
Encapsulation
Standards
Explosives
Ion mobility spectrometry

ABSTRACT

We present a methodology for fabricating polymer microspheres using inkjet printing of a biodegradable polymer containing either high explosives or high explosive simulant. Poly(DL-lactide/glycolide) 85:15 (PLGA) microsphere production is based on an oil/water emulsion solvent extraction process. The inkjet printing process allows for precise control of the microsphere diameter and the chemical composition. The microspheres can be used as calibrants or verification standards for explosives trace detection instruments. Gas chromatography/mass spectrometry analysis demonstrated that the composition of the microspheres was consistent with predicted concentrations based on the amount of analyte incorporated into the polymer solution and the inkjet operating parameters. We have demonstrated that the microspheres can be fabricated with a mass fraction of 70% of an analyte compound.

1. Introduction

Current national priorities in homeland security have led to the widespread deployment of explosives trace detection systems throughout the United States. In a typical implementation of such a detection system, an ion mobility spectrometer (IMS) is used to identify micrometer sized explosive particles on people and their belongings [1]. Samples are typically collected by physical swiping of a suspect surface with a hand wand or small piece of cloth (called a trap). After sampling, the trap is inserted into the IMS instrument where the particles of interest on the trap are thermally vaporized and analyzed. This method is effective for screening objects like a briefcase or a laptop computer, but it is not optimal for screening people or their clothing and is also slow and limited in sample throughput. To address these issues, another approach currently being deployed is the walk-through portal detection system. In this system, a person enters a chamber similar to a metal detector, and is interrogated with multiple air jets that dislodge particles from the person and/or their clothing. An air shower stream carries the dislodged particles to a collector, which in turn admits this material to a detector (generally an IMS) [2].

In order to characterize and validate the performance of these systems, well-characterized test materials are required. Explosives residues are typically found as small particulates with size distributions ranging from sub-micrometer to several 100 μm in diameter [3]. In order to make realistic standards to serve as effective test materials for trace detection instruments, particulate test standards should have several desirable properties: appropriate size and aerodynamic behavior; known chemical composition; known surface adhesive properties; a distinguishable IMS detector response. Particle size is particularly important because particle release from surfaces by air jets and aerodynamic transport are particle diameter-dependant [4,5]. Some additional considerations include useful lifetime of the standard in the local ambient environment, contamination control at the test site that results from standard testing, and the safety (non-toxicity) of the materials in the event of accidental human exposure.

One novel and promising method for generation of these trace particle standards is the production of uniform polymer microspheres containing the explosive compound (or simulant) of interest by inkjet printing. The use of polymer microspheres is advantageous because they are monodisperse, the sphere diameters can be tailored for specific tests, and the microspheres may contain high levels of test compound.

* Corresponding author at: National Institute of Standard and Technology, Chemical Science and Technology, 100 Bureaue Drive Stop 8371, Gaithersburg, MD 20899, United States. Tel.: +1 301 975 3912.
E-mail address: robert.fletcher@nist.gov (R.A. Fletcher).

0039-9140/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.talanta.2008.04.066

In this paper, we present a methodology for fabricating uniform polymer microspheres by using inkjet printing of a biodegradable polymer containing the compound of interest. This approach was originally developed for drug delivery applications using inkjet printing of a polymer solution containing poly(DL-lactide/glycolide) (PLGA) and paclitaxol [6,7]. Here we use a similar approach for preparing PLGA spheres containing high explosives or a simulant. Uniform microspheres have been made by piezoelectric fluid flow disruption over 35 years ago [8]. Production is based on an oil/water emulsion solvent extraction process that produces polymer microspheres [9]. Others have presented methods for making drug delivery microspheres, using a co-flow polymer/water system [10]. One reason to incorporate drugs into polymer microspheres (PLGA and polylactide, PLA) is that the polymer slowly degrades or dissolves by hydrolysis in the body to provide a slow release drug delivery platform [11–13].

We have demonstrated the incorporation of two high explosives, 1,3,5,7-tetranitroperhydro-1,3,5,7-tetrazocine (HMX) and 2,4,6 trinitrotoluene (TNT), and one simulant, 2,6-bis(1,1-dimethylethyl)-4-methylphenol (BHT, CAS number 128-37-0), into PLGA microspheres. We are using the simulant BHT because it is a food additive, considered safe for human consumption and gives a good IMS response in the negative ion mode where explosives are detected. A safe simulant is desirable to prevent contamination of the security check points and to prevent potential health risk from accidental human exposure. The above analytes contained in the PLGA microspheres have been correctly identified for the respective compound by a table-top IMS.

2. Experimental

2.1. Materials

The polymer solution was made by dissolving either 0.3 g or 0.6 g of poly(DL-lactide/glycolide) 85:15 (PLGA, Polysciences Inc., Warrington, PA)[1] into 10 mL dichloroethane (DCE) (Sigma–Aldrich, St. Louis, MO). Low and high concentration solutions of BHT (Sigma–Aldrich, St. Louis, MO) were made by dissolving either 0.07 g or 5 g BHT into 10 mL DCE. HMX was first dissolved in acetone (J.T. Baker) and then the acetone solution was added to the DCE to make a 2.73×10^{-4} g/mL HMX solution in DCE–acetone. For a low concentration solution of TNT, 0.025 g of TNT was dissolved in 10 mL DCE. A final solution of polymer and analyte was made by mixing a known volume of analyte solution into the PLGA–DCE solution. Approximately 200 μL of rhodamine B (Eastman Kodak Co., Rochester, NY) was also added to the final polymer–analyte solution as a fluorescent dye marker.

2.2. Microsphere fabrication

Microspheres were prepared by an oil/water emulsion process using a piezoelectric inkjet printer (sphere jet) to deliver precisely controlled microdrops of the polymer solution. The sphere jet is a drop-on-demand piezoelectric inkjet printer (MicroFab Technologies Inc., Plano, TX) with a 50-μm orifice diameter jet, operated in a pressure assisted mode to prepare PLGA microspheres containing analytes of varying concentrations. A magnified image of the inkjet printer producing a stream of monodisperse droplets

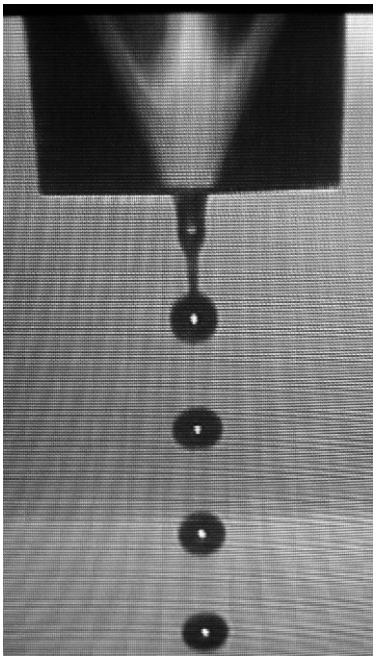

Fig. 1. Inkjet printer operating in a continuous mode producing uniform droplets.

is shown in Fig. 1. The waveform and frequency were controlled using the instrument's software (JetLab2) and pressure regulation was maintained using a pressure regulator (Druck DPI 530, Druck Inc., Fairfield, CT). Operating parameters were varied to allow for controlled production of microspheres, but typical parameters include a frequency of 10 kHz, rise time 1 μs, dwell time 30 ms, and dwell voltage of 30 V. A video camera with strobe illumination (Advanced Illuminations, Signatech, Rochester, VT) was used to monitor the shape and relative size of the jetted droplets. The pressure-controller driven stream of the polymer solution flowed through the inkjet tip forming microspheres as a result of uniformly disrupting (or chopping) the stream by the capillary piezoelectric tip. The jetting process takes place under water where the microspheres are captured and cured in a 500-mL beaker (containing filtered, deionized water) continuously stirred for several minutes to several hours. Any DCE that remained after sphere formation was allowed to evaporate. Using vacuum filtration, a small volume (approximately 25 mL) of the microsphere suspension was filtered through a 25-μm diameter polycarbonate filter with a 1.0-μm pore size and the remaining solution was filtered through a 47-μm polycarbonate filter with a 1.0-μm pore size. Optical microscopy was used to image the microspheres collected on the 25 mm filter and the microspheres collected on the 47 mm filter were dried and carefully removed from the filter using a spatula and stored in 5 mL closed vials.

Three different jetting experimental configurations were examined as a way to reduce the variability of the microsphere size distribution. The first configuration is considered a "pure-shear" mode because the piezoelectric nozzle is directly submerged in the 500 mL beaker filled with rotationally stirred water. The droplets are immediately sheared from the nozzle by the rotating body of water. The limitation of this method is that it makes it difficult to focus the camera on the nozzle and droplets because of the curved walls of the beaker. Configurations 2 and 3 were designed to overcome this visualization issue by using a co-flow tube with flat glass walls (see Fig. 2a and b). Results of these three arrangements will be discussed later.

[1] Commercial equipment, instruments, and materials, or software are identified in this report to specify adequately the experimental procedure. Such identification does not imply recommendation or endorsement of these items by the NIST, nor does it imply that they are the best available for the purpose.

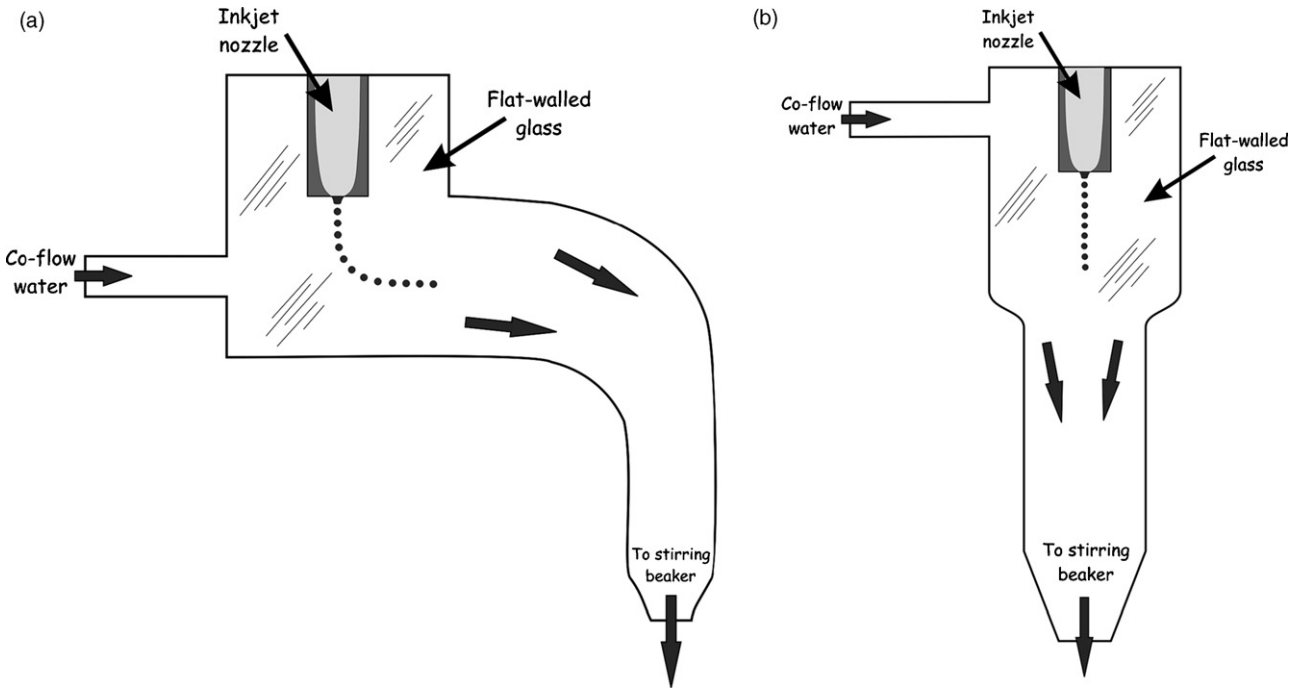

Fig. 2. Arrangement 1, not shown, was directly submerging the nozzle in a rotating beaker of water. Curved co-flow nozzle (a) is arrangement 2 and straight co-flow nozzle (b) is arrangement 3. Particles are generated by the submerged inkjet printer and are carried by a continuous stream of water into a collection beaker where they are left to cure.

2.3. Experimental design: fabrication parameters

An experimental design was followed that included a wide range of operating conditions for microsphere production by the sphere jet. The relevant parameters related to producing spherical particles of a given diameter from the sphere jet are the solute concentration, the liquid flow rate and the operating frequency of the jet. We varied the solute concentration for PLGA in DCE (0.06 g/mL and 0.12 g/mL), the BHT (0.014 g/mL and 1 g/mL), the frequency (5 kHz, 10 kHz and 20 kHz), and the flow rate through the jet from 0.0022 mL/s to 0.0069 mL/s. The experimental parameters allow us to predict the resultant sphere diameter and compare this value to the measured diameter.

2.4. Characterization of the microspheres

2.4.1. Optical microscopy

The microspheres were imaged using a fluorescence optical microscope (Zeiss Stemi SV 11) for analyses of the microsphere diameter and degree of monodispersity. Samples which showed obvious polydispersity were not included for further study. The mean diameter of selected spheres in monodisperse samples was calculated using image analysis (ImagePro Software [Media Cybernetics Inc.]). Individual spheres were sized while the sizes of clusters or agglomerations of spheres were rejected due to the inability of the program to differentiate individual spheres. However, visual inspection indicated that the size of microspheres in clusters matched the microsphere sizes of the individual spheres.

2.4.2. Microsphere size distribution

A known volume of microspheres in aqueous suspension was sized by an optical particle counter that utilizes single particle optical extinction (model HR LD 150, HACH ULTRA, Grants Pass, OR). The instrument was calibrated with polystyrene latex spheres (Duke Scientific), over the size range from 1 μm to 100 μm. It is important to note that the micrograph images of the microspheres are of filtered and dried microspheres, which were observed to agglomerate while the optical particle counter performed the measurement in suspension, where the particles did not appreciably aggregate. A Coulter Multisizer 3 (Beckman Coulter Inc.) with a 100-μm orifice was used to measure the size distribution of certain cured PLGA spheres.

2.4.3. Scanning electron microscopy

Microspheres were sputter coated with a thin layer of gold. Spheres were viewed using a field emission scanning electron microscope. Some of the samples were imaged at an acute angle to examine contact angle of the sphere attachment to the surface.

2.4.4. Gas chromatography–mass spectrometry analysis

A known mass (1.30 mg) of the HMX in PLGA sample was transferred to a 2-mL amber vial to which was added a known mass of a solution of deuterium labeled HMX (Cambridge Isotope Laboratories, Andover, MA) and approximately 1 mL of acetone (J.T. Baker, Baker's Analyzed HPLC solvent). A known mass of a standard HMX solution was fortified with the same labeled-HMX solution as the sample. This solution was used as a calibrant to determine a response factor for the HMX relative to the labeled compound (see below).

For the BHT in PLGA sample, 2.43 mg was deposited into a 2-mL amber vial and the material was dissolved in approximately 1 mL of acetone (described above). For the BHT calibration, a solution at a similar concentration to that predicted from the sample composition was prepared from pure BHT (Sigma, St. Louis, MO). The calibrant was used to generate a response factor relating the amount of BHT injected to the area of the resulting BHT chromatographic peak.

The HMX and BHT concentrations were determined by gas chromatography/negative ion chemical ionization mass spectrometry (GC/NICI-MS) using an Agilent 6890 GC system interfaced with an Agilent 5973 MS. Aliquots of the extracts (1 μL) were injected by an autosampler onto a 1 m × 0.25 mm uncoated/deactivated fused sil-

ica capillary (retention gap) connected to a 6 m × 0.22 mm (0.1 μm phase, SGE, Austin, TX, serial number 9835C15) HT-5 column. The retention gap-column combinations were operated at a constant flow rate of 14 mL/min helium, and temperature programmed from 80 °C (1 min hold) to 100 °C at 45 °C/min, then to 170 °C at 5 °C/min (10 min hold). The mass spectrometer was operated in the NICI mode with methane as the reagent gas (40 mL/min), scanning from 40 to 350 mass/charge (m/z) for the BHT measurements and monitoring for ions 176 m/z (HMX) and 181 m/z (labeled-HMX) for the HMX measurements. The source and analyzer temperatures were set at 150 °C and 200 °C, respectively, and the MS was tuned prior to the sample runs. Peak areas of reconstructed ion chromatograms for 176 m/z, 181 m/z and 219 m/z (BHT) were used to determine relative response factors from calibrant runs that were then used to quantify the concentrations of BHT and HMX in the prepared solutions. The precision of the methods suggests a run-to-run uncertainty of approximately 5%. The uncertainty due to heterogeneity in the materials was not addressed in this work due to limitations in the amount of sample available.

2.4.5. Ion mobility spectrometry (IMS)

Weighed amounts of microspheres incorporated with BHT and TNT were analyzed using a commercial IMS (Itemiser 3, GE Security) operated with a 220 °C desorber temperature. For microspheres incorporated with HMX, an IonScan 400B (Smiths Detection) was used with a 280 °C desorber temperature. IMS plasmagrams of the microspheres were obtained for analysis.

3. Results and discussion

One of the primary advantages of using the piezo inkjet approach compared to conventional methods of emulsion polymerization methods is that monodisperse microspheres can be made that contain the same amount of analyte per sphere, which is critical if it is to be used as a test material. In the current implementation, the inkjet is used in a continuous mode. The polymer solution is pushed continuously through the nozzle by a constant applied back pressure. We produce a uniform stream of polymer solution and apply a waveform to drive the piezoelectric crystal in the frequency range of 5–20 kHz. Uniform liquid stream break-up behavior is described [10,14]. There is similarity between our particle generation device and a well-known aerosol particle generator, the vibrating orifice aerosol generator. The aerosol generator sends a chopped stream into air or gas and the present device streams into water. The droplet diameter, d_d, can be predicted by the following expression:

$$d_d = \left(\frac{6Q}{\pi f}\right)^{1/3}, \quad (1)$$

where Q (mL/s) is the liquid flow rate and f is the disruption or chopping frequency. The final particle diameter, d_p is controlled by the volumetric concentration of solute present, C, in the solution and expressed as

$$\frac{d_p}{d_d} = C^{1/3}. \quad (2)$$

We designed a fabrication experiment that included high and low concentrations for PLGA, BHT and various applied chopping frequencies. Using Eqs. (1) and (2) and measuring the solute concentration and the liquid flow rate, we are able to calculate the expected particle diameter. Fig. 3 shows a scatter plot of calculated particle diameters versus those measured by optical microscopy. This data is for both BHT and HMX containing PLGA spheres and excludes any samples not deemed monodisperse. The plot shows that although the predictability is not ideal, we do have control of particle and composition by varying the operation parameters for the fabrication.

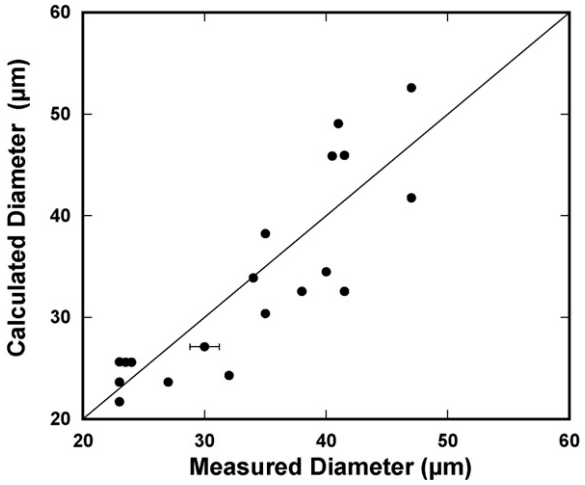

Fig. 3. Scatter plot of calculated sphere diameter versus measured sphere diameter. The line is a 1:1 relation drawn for comparison. The uncertainty bar corresponds to standard deviation in the measured diameter.

A typical fluorescence micrograph of nominal 30 μm diameter PLGA spheres containing BHT and rhodamine B are shown in Fig. 4. The spherical shape and uniformity are evident. The particles appear to be agglomerated due to filtering from the suspension. A scanning electron micrograph of the microspheres is shown in Fig. 5. The particles are mounted on a silicon wafer, coated with a thin gold coat and imaged at an acute angle. The particles appear to be rigid, well defined spheres. This imaging technique allows verification of the shape to a much finer degree and also visualization of any defects or residues that could be on the sphere's surface or at the sphere–substrate interface.

The particles were characterized in suspension using an optical particle sensor based on light extinction described above. The extinction sensor was calibrated using monodisperse polystyrene spheres. The extinction sensor provides a quick diagnostic tool to obtain the relative size of the microspheres and the breadth of the size distribution while the spheres are in suspension. An example of a measurement is presented in Fig. 6 that shows a single peak at a sphere diameter of approximately 20 μm. Over 64,000 particles were characterized to make this plot. The sample was made

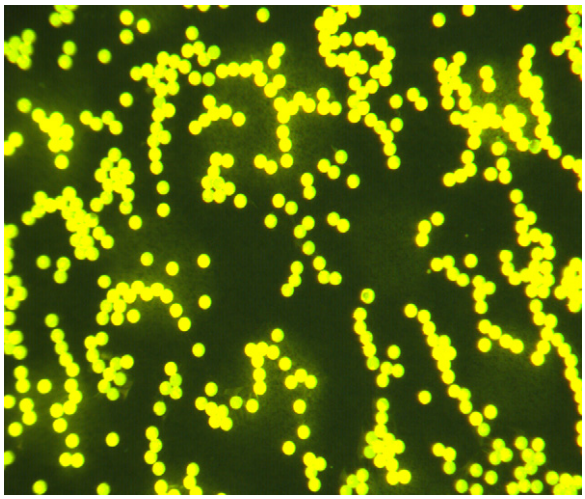

Fig. 4. Fluorescence micrograph of PLGA spheres containing BHT and rhodamine B.

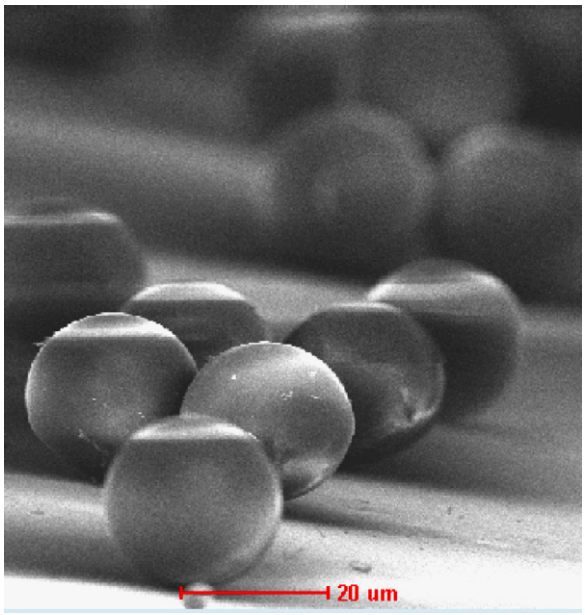

Fig. 5. SEM micrograph of PLGA–BHT spheres viewed at an acute angle with respect to the substrate.

from a 0.03-g/mL PLGA solution containing 0.007 g/mL BHT with the inkjet operating at a frequency of 20 kHz. The full-width half-max of the peak is approximately 2 μm, indicating approximately 10% dispersion in the particle diameter using this method.

In order to optimize the fabrication process, polymer microspheres produced from the three jetting arrangements (see Fig. 2) were analyzed by the Coulter counter to determine the size distribution of the sphere population. In the arrangements shown in Fig. 2a and b, the polymer droplets would travel with the co-flow fluid through the tube. However, the fluid flow rate was not high enough to keep the droplets separate and a fraction of the droplets began to coalesce into larger droplets before curing and hardening. Coalescence occurred as a repeating process of two droplets forming a larger droplet all along the transport tube until finally settling into the beaker. The results of droplet coalescence is shown in Fig. 7. Multiple peaks are in fact derived from coalescence of droplets as evidenced by the fact that the peaks scale as multiples of the cube root of the number of droplets coalescing (n) times the initial diameter ($n^{(1/3)} \times$ diameter; for $n = 1, 2, 3, \ldots$).

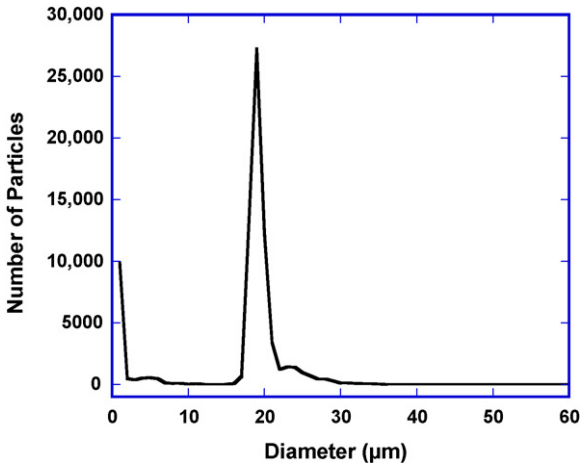

Fig. 6. Relative particle diameter obtained for suspended PLGA spheres containing BHT. Measurements were made using the optical extinction particle sensor.

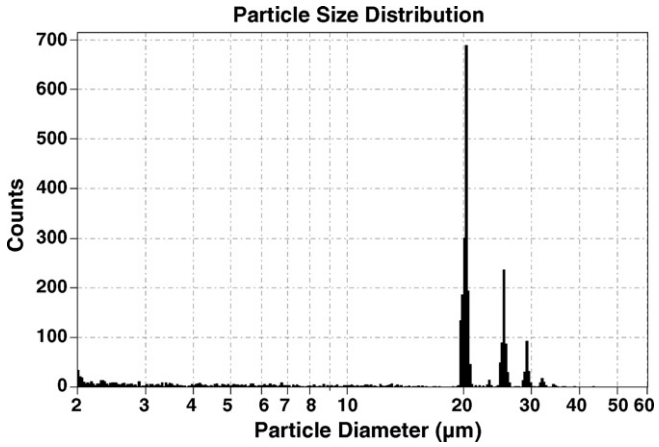

Fig. 7. Particle size distribution of PLGA spheres for co-flow nozzle shown Fig. 2a and b, arrangements 2 and 3. Multiple peaks indicates coalesce of the microspheres prior to curing while the droplets are still the liquid phase.

Submerging the nozzle directly into the stirring water (arrangement 1) was the only way to eliminate the coalescence problem. Fig. 8 shows a typical size distribution plot for arrangement 1 (jetting directly into the beaker). The mean is 19.43 μm with a standard deviation of 0.29 μm (number of spheres is 1260). The coefficient of variation is 1.5%, which is comparable to commercially available materials, such as NIST standard reference material polystyrene latex microspheres.

Another set of spheres was made from solution concentrations of 0.06 g/mL PLGA with 0.007 g/mL BHT and an operating frequency of 20 kHz was analyzed using fluorescence light microscopy and image analysis. The particles were collected on a polycarbonate filter and were agglomerated due to the filtration process. Using a deagglomeration feature of the image analysis software, 175 spheres were selected at random and sized. The results of image analysis are shown in Fig. 9. The mean of this population was 29.32 μm with a standard deviation of 1.15 μm.

The polymer's capacity to degrade thermally is very important for the proposed application. The PLGA spheres should release the high explosive or simulant when heated during the trace analysis technique. Also, the ions formed from the polymer degradation could become potential interference peaks for the IMS. Fortunately, it was observed that PLGA does not produce any interfering peaks in the negative or positive ion mode for IMS. Measurements at

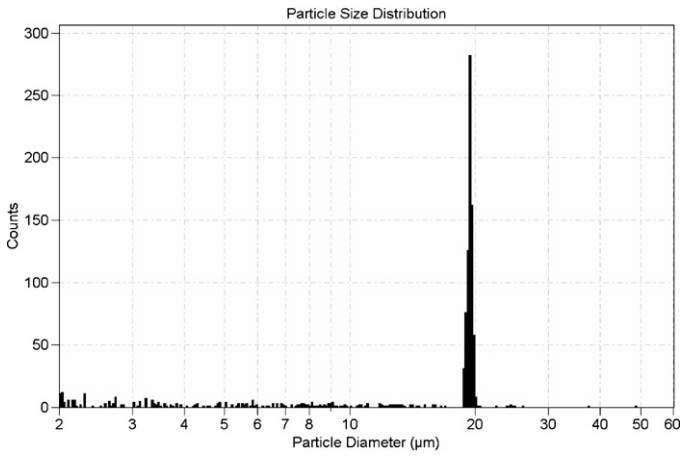

Fig. 8. Particle size distribution of PLGA sphere obtained for jetting arrangement 1 where the droplets are deposited directly in a rotating water bath. No coalescence is observed.

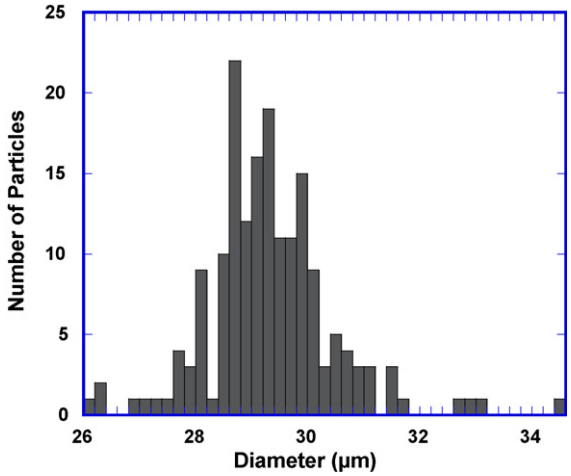

Fig. 9. Histogram representation of PLGA–BHT spheres sized by fluorescence microscopy and image analysis.

NIST and in the literature indicate that PLGA does not thermally degrade before 300 °C [15]. All three analytes TNT, HMX and BHT incorporated in PLGA have been detected by IMS without further preparation other than heating the spheres in the IMS desorber. Desorber temperatures were either 220 °C or 280 °C depending upon the analyte analyzed. Although elevated temperatures were used to desorb HMX, they are not necessary to melt the PLGA spheres. Experiments on a controlled hot stage indicate that the PLGA microspheres melt between 100 °C and 130 °C leaving a visible residue. Using Eq. (2), we can calculate the amount of explosive or simulant in each sphere. Given a final sphere diameter of 30 μm fabricated from the dilute HMX solution specified above with the 0.03 g/mL PLGA solution, we arrive at an inkjet ejected drop diameter of approximately 111 μm. With the solution containing 4.5×10^{-5} g/mL, we obtain approximately 32 pg of HMX in each sphere. The mass of HMX per sphere is so small (trace) that we needed multiple spheres with this concentration to detect HMX by IMS.

The temporal variation of characteristic ions observed in IMS provides information of both the compound desorption rate and detection. A plot of $(HMX - Cl)^-$ peak height as a function of time for pure HMX and for HMX desorbed PLGA–HMX is shown in Fig. 10.

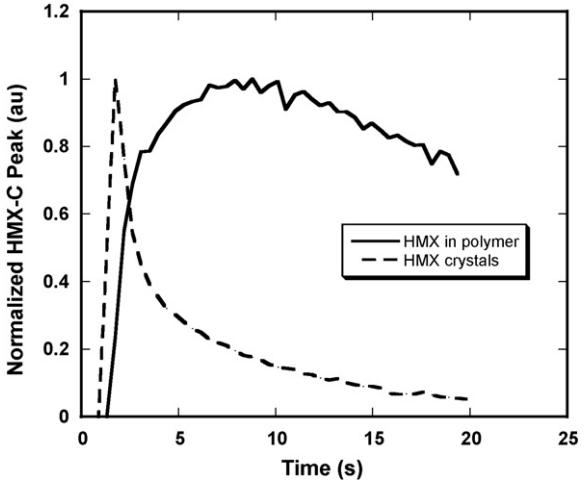

Fig. 10. IMS response for approximately 20 ng of pure HMX and HMX incorporated in PLGA spheres. The peak height $(HMX + Cl^-)$ is normalized to the maximum in the scan and plotted as a function of desorbtion time.

The pure HMX was deposited and dried from DCE solution onto a sample trap. In both cases the IMS operating conditions and sample trap were the same. The pure HMX compound (approximately 20 ng) desorbs nearly completely in the first few seconds, peaks at approximately 3 s and then decays. The HMX signal derived from the HMX–PLGA spheres takes about 8 s to reach maximum and stays fairly constant out to 20 s, the duration of the analysis scan. The fact that the polymer appears to retain some of the explosive compound is not surprising and does not negate the applicability of this technique. In fact for some volatile compounds the slow thermal release may be beneficial for molecular preservation and stability of the compound. Further testing will be needed to quantify the thermal release rate from the polymer.

Preliminary results for the final concentrations of HMX and BHT in two PLGA sphere samples as determined by GC/NICI-MS suggest that the observed levels are close to those predicted by the formulations. Duplicate injections of the HMX in PLGA dissolved in acetone yielded concentrations of 1204 μg/g and 1213 μg/g HMX, in good agreement with the range of predicted levels of 1820 μg/g. The result for the BHT in PLGA sample was somewhat lower than predicted, with the GC/NICI-MS measurement yielding a concentration of about 0.71 g/g, or mass fraction of 71% BHT compared with the predicted mass fraction of 76% BHT. We estimate that there is approximately 10% uncertainty in the results. As indicated above, sample limitations prevented a thorough determination of the homogeneity of the analytes in the PLGA polymer, but these preliminary results do suggest the proof-of-concept of generating known levels of HMX and BHT in the PLGA material by the method described above.

4. Summary

There is a need for test particles of high explosives and their simulants for testing IMS based trace portal systems. We have developed a potential method to produce particle-based standard test materials at the trace levels for IMS portal systems. Two high explosives and one high explosive simulant were incorporated into PLGA biodegradable polymer microspheres using inkjet printing. The design parameters, i.e., the solution concentrations, feed rate and inkjet operating frequency largely control the outcome regarding microsphere size. We have demonstrated that 70% (by mass) of the microsphere can contain the BHT simulant. When incorporated into PLGA, explosive compounds can be detected by an IMS and there is compatibility of PLGA with the IMS in the negative ion mode. The concentrations determined for HMX and BHT analytes residing in the PLGA spheres are close to the predicted values based on dilution ratios. To our knowledge, this is the first time high explosive compounds have been incorporated into PLGA microspheres. Additional testing will be necessary to quantify the polymer retention rate of various compounds during heating. Further studies have been initiated to compositionally map the PLGA microspheres to understand the degree of spatial uniformity present in the polymer material. There are ongoing tests to determine the stability of the microspheres and other materials will be examined to determine their feasibility for trace explosives test standards application.

Acknowledgements

The Department of Homeland Security sponsored the production of this work under an interagency agreement with the National Institute of Standards and Technology. The authors would like to acknowledge helpful discussions with Dr. Cory Berkland.

References

[1] R.G. Ewing, D.A. Atkinson, G.A. Eiceman, G.J. Ewing, Talanta 54 (3) (2001) 515–529.
[2] S. Hallowell, Talanta 54 (2001) 447–458.
[3] J.R. Verkouteren, J. Forensic Sci. 52 (2) (2007) 335–340.
[4] M.B. Ranada, Aerosol Sci. Technol. 7 (1987) 161–176.
[5] A.D. Zimon, Adhesion of Dust and Powder, Consultants Bureau, New York, A Division of Plenum Publishing Corporation, New York, NY, 1982.
[6] D. Radulscu, N. Schwade, D. Wawro, Proceedings of the 11th International Symposium on Recent Advances in Drug Delivery Systems, Salt Lake City, UT, 2003.
[7] D. Radulescu, H.J. Trost, D. Taylor, B. Antohe, N. Schwade, P. Tarcha, D. Silva, S. Dhar, G. Evans, Proceedings of the Image Science and Technology DF05, the International Conference on Digital Fabrication Technologies, Baltimore, MD, 2005.
[8] M.J. Fuwyler, J.D. Perrings, L.S. Cram, Rev. Sci. Instrum. 44 (2) (1973) 204–206.
[9] P.B. O'Donnel, J.W. MacGinity, Adv. Drug Deliv. Rev. 28 (1997) 25–42.
[10] C. Berkland, K. Kim, D. Pack, J. Control. Release 73 (2001) 59–74.
[11] D.T. Birnbaum, L. Brannon-Peppas, in: D.M. Brown (Ed.), Microparticle Drug Delivery Systems in Drug Delivery Systems in Cancer Therapy, Humana Press, Inc., Totowa, NJ, 2003.
[12] C. Berkland, K. Kim, D. Pack, Pharm. Res. 20 (7) (2003) 1055–1062.
[13] C. Raman, C. Berkalnd, K. Kim, et al., J. Control. Release 103 (2005) 149–158.
[14] R. Berglund, B.Y.H. Liu, Environ. Sci. Technol. 7 (1973) 147–153.
[15] A.A. Silva-Junior, M.V. Scarpa, K.C. Pestana, L.P. Mercuri, J.R. de Matos, A.G. de Oliveira, Thermochim. Acta 467 (1/2) (2008) 91–98.