Physico-chemical Characterization of Extracts of Silver Nanoparticle Containing Medical Devices

B.J. Casey[1,*], P. Jayanti[1,**], E.M. Sussman[1,***] and B.J. Dair[1,****]

[1]United States Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Laboratories, Division of Chemistry and Materials Science, 10903 New Hampshire Avenue, Silver Spring, MD, USA

[*]brendan.casey@fda.hhs.gov, [**]priyanka.jayanti@fda.hhs.gov, [***]eric.sussman@fda.hhs.gov, [****]benita.dair@fda.hhs.gov

ABSTRACT

The main goal of this research was to gain a better understanding of the extraction profile of medical devices containing silver, specifically nanosilver. Multiple silver containing medical devices were incubated in various extract solutions (water, 0.9% saline, human plasma) under multiple conditions (1 hour, 24 hours, 168 hours @ 37°C; 72 hours @ 50°C). Inductively coupled plasma – mass spectrometry (ICP-MS) was used to determine the total amount of silver which had leached from the devices. Dynamic light scattering (DLS), ultraviolet-visible light spectroscopy (UV-Vis), nanoparticle tracking analysis (NTA) and transmission electron microscopy (TEM) were utilized to characterize the physical structure of the particulates released from the devices. Field emission scanning electron microscopy (FESEM), and corresponding energy dispersive x-ray spectroscopy (EDS) were used to image and analyze the elemental composition of the surface of each medical device.

This research has provided insight into the both the amount and physical form of silver that is released from silver containing medical devices. The data from this research is currently being implemented into a risk assessment model which will be used to better assess the safety and efficacy of medical devices which contain silver nanoparticles.

Keywords: Nanosilver, silver nanoparticle, medical device, leachate, physico-chemical characterization

1 INTRODUCTION

The use of nanotechnology, specifically silver nanoparticles, within medical devices has dramatically increased over the past decade. Silver nanoparticles are antimicrobial, have a high surface area to volume ratio, and can easily be incorporated into medical device materials, e.g. polymers. Another benefit of silver nanoparticles is their ability to continuously release silver ions, the active antibacterial agent, which results in an extended antimicrobial effect. Silver nanoparticles have been incorporated into a broad range of medical devices including catheters, dental resin composites and wound dressings [1-3]. Due to the increased use of silver nanoparticles in medical devices it is important that the scientific and regulatory community develop an understanding of the biological interaction of silver nanoparticles in order to better assess safety and efficacy.

2 METHODS

2.1 Characterization of Medical Devices

A small sample of each silver containing medical device was attached to a metal platform with conductive carbon tape. Each of the samples were then sputter coated with carbon for approximately 1 minute. The samples were then imaged using FESEM (Hitachi SU-70 FESEM). Operating voltage ranged from 5-15 keV. EDS (Bruker Quantax XFlash Detector 4010) was completed on various parts (surface) of each of the medical devices to confirm the presence of silver.

2.2 Characterization of Leachates

Small samples of silver containing medical devices were incubated in various extract solutions (water, 0.9% saline, human plasma) under multiple conditions (1 hour, 24 hours, 168 hours @ 37°C; 72 hours @ 50°C). Three separate trials were completed and analyzed (n=3). After each respective time point a sample of the leachate solution was extracted and analyzed using ICP-MS (Thermo Scientific XSERIES 2), DLS (Malvern Zetasizer Nano ZS), NTA (NanoSight NS500), UV-Vis (Molecular Devices Spectra MAX 190) and TEM (JEOL JEM-1011) with corresponding EDS (Oxford Instruments X-Max^{N} 80 T).

NSTI-Nanotech 2014, www.nsti.org, ISBN 978-1-4822-5830-1 Vol. 3, 2014

3 RESULTS

3.1 Characterization of Medical Devices

FESEM, along with corresponding EDS analysis, was used to characterize the surfaces of the various silver containing medical devices investigated in the study. Figure 1 below contains surface images of 2 of the devices investigated in this study. Both of the images (A and B) shown below in Figure 1 are types of wound dressings. Nanofeatures can clearly be seen on both wound dressing surfaces, but they are more prominent on wound dressing #1 (Figure 1A). Nanofeatures on the surface of the wound dressing #1 (Figure 1 A) are approximately 20-50 nm in size. EDS of each surface confirmed the presence of silver on each surface.

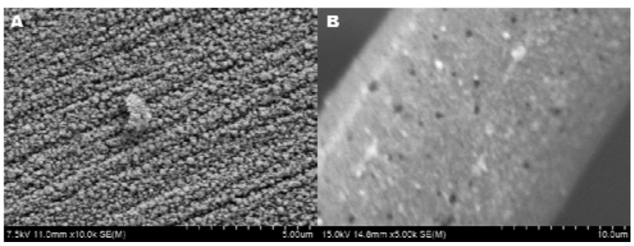

Figure 1: A) FESEM image of a silver containing wound dressing (wound dressing #1). B) FESEM image of a silver containing wound dressing (wound dressing #2).

3.2 Characterization of Leachates

As stated previously, small samples of different silver medical devices were incubated in various extract solutions (water, 0.9% saline, human plasma) under multiple conditions (1 hour, 24 hours, 168 hours @ 37°C; 72 hours @ 50°C). After incubation the samples (leachate solutions) were analyzed to determine the total amount of silver (ICP-MS). Physico-chemical characterization (DLS, NTA, UV-Vis, TEM) was completed to identify the type of silver species, e.g. ionic or nanoparticulate, released by the medical devices.

The amount of silver released by each medical device in the first hour was far greater than the amount of silver released in the subsequent hours for each of the extract solutions (water, 0.9% saline, human plasma). In most cases greater than 80% of the total silver released by the device after 168 hours (7 days) of incubation was released in the first hour. The data indicates that most silver impregnated or coated devices exhibit a burst release of silver upon initial introduction to an aqueuos solution. This burst release of silver is most likely caused by two primary factors: 1) rapid dissolution (oxidation) of metallic silver into silver ions (Ag+) in an aqueous environment 2) silver is located on the surface of most of the devices tested (coating).

ICP-MS analysis of the various leachate solutions also showed that the amount of silver released is highly dependent on the device. The dependence of silver release on device type is mostly likely due to the varying amounts of silver incorporated into each device along with the fact that different materials will interact with silver differently. Previous research has shown that silver release is influenced by the material to which it is coated on, e.g. some materials having a stronger interaction/association with silver species resulting in less release [4].

In addition to the total amount of silver released, physico-chemical analysis was completed to gain a better understanding of the species of silver leached from the devices. DLS, NTA, UV-Vis and TEM/EDS were utilized to characterize the type of silver being released from the various devices, i.e. ionic or particulate. Figure 2 below shows a representative TEM image of a leachate solution obtained after incubation of a silver coated wound dressing (wound dressing #1). As shown in Figure 2 below, various shapes and sizes of silver nanoparticles were observed in the leachate solution of this particular wound dressing. The nanoparticles ranged in size from approximately 5-100 nm. The presence of nanoparticles was supported by further analysis, specifically DLS and NTA. Although it was apparent that silver nanoparticles were contained within the leachate solution it was unclear whether these nanoparticles leached, as a whole, from the wound dressing or whether they formed in solution via the reduction of released silver ions. The reduction of silver ions in solution to form nanoparticles is a well known phenomonon and has been studied and documented in prior research within the laboratory.

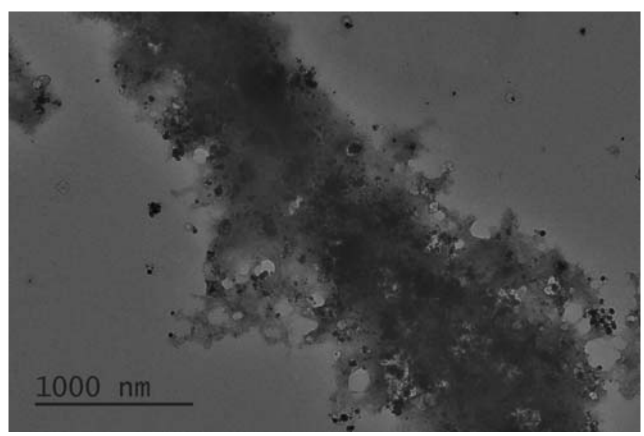

Figure 2: TEM image of leachate solution obtained after extraction of a nanosilver containing wound dressing (wound dressing #1). Ten (10) µL of the leachate solution was added directly to a TEM grid and imaged accordingly.

Similar to silver release (ICP-MS analysis), the researchers found that the type/species of silver released was highly dependent on the device. In several of the samples the presence of silver nanoparticles could not be established. ICP-MS analysis confirmed that all the samples did leach some amount of silver in either water, 0.9% saline or human plasma. The fact that nanoparticles were only identified in a few leachate solutions suggests that the nanoparticles were actually released from these devices and not formed via ion reduction, yet this was not thoroughly investigated.

4 CONCLUSION

FESEM along with corresponding EDS analysis was utilized to characterize the surface structure of various silver containing medical devices. In almost all cases, the presence of nanostructured silver features could be identified. The medical devices were all extracted under a variety of conditions to better understand the amount and type of silver which would be released in a physiological environment. ICP-MS analysis of the leachate solutions indicated that silver, in some form, was released from all devices under invetigation. The experimental results indicate that the amount and form of silver released is dependent upon the device along with the phyisological environment, i.e. incubation conditions. Subsequent physico-chemical analysis of the solutions established the presence of silver nanoparticulates within the leachate solutions of some of the medical devices. The fact that the nanoparticles were not identified in all leachate solutions suggested that the nanoparticles were being leached from the device(s) as a whole and not formed via reduction of silver ions in solution. The results of the work are crucial to develop a better understanding of nano(silver) containing medical devices. A better understanding of nano(silver) coated devices and how they interact with the body will allow the scientific community to better assess the safety and efficacy of products containing nano(silver).

Disclaimer: The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services.

REFERENCES

[1] Bayston, R.; Vera, L.; Mills, A.; Ashraf, W.; Stevenson, O.; Howdle, S. M. In vitro antimicrobial activity of silver-processed catheters for neurosurgery. *Journal of Antimicrobial Chemotherapy*, 65, 258-265, 2010.

[2] Kostenko, V.; Lyczak, J.; Turner, K.; Martinuzzi, R. J. Impact of Silver-Containing Wound Dressings on Bacterial Biofilm Viability and Susceptibility to Antibiotics during Prolonged Treatment. *Antimicrobial Agents and Chemotherapy*, 54, 5120-5131, 2010.

[3] Samuel, U.; Guggenbichler, J. P. Prevention of catheter-related infections: the potential of a new nano-silver impregnated catheter. *International Journal of Antimicrobial Agents*, 23, S75-S78, 2004.

[4] Dair, B. J.; Saylor, D. M.; Cargal, T. E.; French, G. R.; Kennedy, K. M.; Casas, R. S.; Guyer, J. E.; Warren, J. A.; Kim, C. S.; Pollack, S. K. The Effect of Substrate Material on Silver Nanoparticle Antimicrobial Efficacy. *Journal of Nanoscience and Nanotechnology*, 10, 8456-8462, 2010.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the University of Maryland Nanoscale Imaging Spectroscopy and Properties Laboratory in addition to Juan Pablo Hurtado Padilla and Wen-An Chiou.