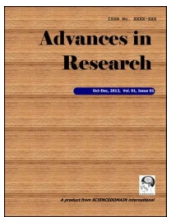


Advances in Research
3(1): 84-91, 2015, Article no.AIR.2015.008
ISSN: 2348-0394

SCIENCEDOMAIN *international*
www.sciencedomain.org

Magnetic Hyperthermia Behavior of Electrospun Polyvinylpyrrolidone (PVP) Nanofibers Containing Magnetic Oxide Materials

Justin Kim[1], Sharon Zhu[1], Yong X. Gan[1*] and Keith Forward[2]

[1]Department of Mechanical Engineering, California State Polytechnic University, Pomona, 3801 W Temple Avenue, Pomona, CA 91768, USA.
[2]Department of Chemical and Materials Engineering, California State Polytechnic University, Pomona, 3801 W Temple Avenue, Pomona, CA 91768, USA.

Authors' contributions

This work was carried out in collaboration between all authors. Authors JK, SZ and YXG designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors JK and YXG did the literature searches, experimental design and data analyses. Author KF performed the SEM experiment. Author YXG managed the project. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AIR/2015/13547
Editor(s):
(1) Francisco Marquez-Linares, Nanomaterials Research Group, School of Science and Technology, University of Turabo, USA.
Reviewers:
(1) Anonymous, Institute of biophysics and biomedicine engineering, Bulagaria.
(2) Manisara Phiriyawirut, Department of Tool and Materials Engineering, King Mongkut's University of Technology Thonburi, Thailand.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=645&id=31&aid=6250

Original Research Article

Received 22nd August 2014
Accepted 8th September 2014
Published 28th September 2014

ABSTRACT

Electromagnetic hyperthermia has been attracting significant attention in treating cancerous cells due to its non-invasive and quick recovery time. In this work, polyvinylpyrrolidone (PVP)solutions containing magnetic materials were used to make nanofibers through electrospinning. Transition metal oxides including cobalt oxide and iron oxide were selected as the magnetic responsive materials. The electrospun magnetic materials containing nanofibers were tested through the exposure to an external electromagnetic field to examine the increase in temperatures. It is found that the temperatures of the nanofibers increased high enough (above 43℃) to damage or eliminate cancer cells within 25 seconds. Comparisons of the hyperthermia behaviors of variousoxideswere studied as well.

**Corresponding author: E-mail: yxgan@csupomona.edu;*

Keywords: Magnetic nanoparticles; electrospinning nanofibers; oxide; external field; hyperthermia.

1. INTRODUCTION

Polyvinylpyrrolidone (PVP) can be dissolved invarious solvents such as ethanol, methanol, dichloromethane to form solutions for electrospinning. Electrospinning can be used to make micro or nanosized PVP nanofibers fairly easily. For example, one-step electrospinning PVP using high pressure carbon dioxide atmosphere has been performed to control the size and the morphology of the obtained fiber product [1]. The electrospun PVP fibers have found many applications including for photoelectronic devices [2], capping AgCl nanoparticles [3], photoluminescence [4], wound healing [5], drug delivery [6], and sensing [7].

Since polyvinylpyrrolidone (PVP) is a water soluble polymer and it has good biocompatibility with human body, it may serve as the bonding agent for holding functional nanomaterials for therapy. Radiation and chemical treatment are used for controlling cancer cells growth [8,9]. These methods damage normal tissues as a result of the high dosage or poisonous drugs used during the treatment processes. A possible solution is the magnetic hyperthermia [10,11]. Besides using iron oxide nanoparticles [12], combinations of several particles including ferrite compounds are considered [13-16]. Hydroxyapatite is also investigated for hyperthermia therapy [17]. Although nanorods [18] and nanoparticles [19] are highly responsive to electromagnetic field as demonstrated before, a biocompatible polymer such as PVP may help the more accurate delivery of the nanoparticles.

The goal of this paper is to prepare superparamagnetic oxide-containing PVP nanofibers and test their hyperthermia properties. Iron oxide, cobalt oxide, and the combination of these oxides with titanium dioxide were in-situ formed in electrospun PVP nanofibers. Theincrease in the temperature of the nanomaterials induced by electromagnetic field was investigated.

2. MATERIALS AND EXPERIMENTAL

2.1 Materials and Instruments

All the materials and reagents used in this work were ordered from Alfa Aesar Company with the ACS purity. The high voltage DC power source module was manufactured by Spellman. The syringes and needles for electrospinning nanofibers were purchased from McMaster Carr Company. The needles were made of brass and coated with nickel. A standard 900 W microwave was purchased from Wal Mart to generate electromagnetic waves for testing the hyperthermia behavior of the nanofibers.

2.2 Preparation of Magnetic Oxides and Electrospinning Nanofibers

The materials selected for this paper were chosen from transition metal oxides, such as iron oxide, cobalt oxide and titanium oxide. Six variations of these oxides were used to create hyperthermia nanomaterials. The following procedures were used to prepare cobalt and titanium oxides. First a small beaker was set on a balance to weight. Then, resetting zero was conducted. After that, the following solutions containing various substances were made using the beaker. 0.13 gram of cobalt (II) acetate tetra-hydrate, $(C_4H_6CoO_4 \cdot 4H_2O \text{ with Co } 24 \text{ wt\%})$, 0.1 gram of 17.4 M acetic acid, 0.17 gram of titanium (IV) n – butoxide, $(C_{16}H_{36}O_4Ti \text{ with } 99 + \% \text{ purity})$, 0.75 gram of polyvinylpyrrolidone powder $(C_6H_9NO)_n$, with the molecular weight of 1,300,000 g/moland 6.8 grams of ethanol(C_2H_5OH) with the ACS purity of 94 – 96% were mixed in the beaker and the solution was stirred to help the solid substances to dissolve into ethanol. After that, an iron oxide containing PVP solution was also made using the similar process.

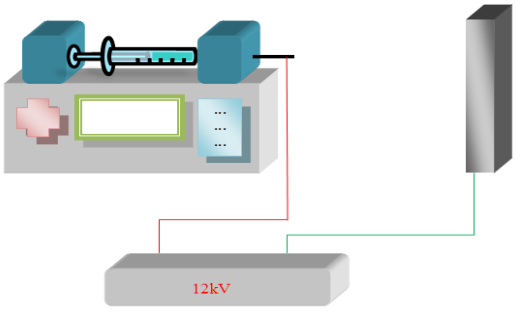
The final solution is highly viscous, a desired property to yield quality nannofibers through electrospinning. The cobalt salt and the titanium organic-compound tend to hydrolysis and produce cobalt hydroxide and titanium hydroxide. After the nanofibers were dried, cobaltoxide and titanium oxide formed. The addition of the little amount of acetic acid was for controlling the rate of hydrolysis to make the reaction not too fast. Once each solid constituent was dissolved into the ethanol, the mixture was poured into a syringe with a needle. The needle has a gage size of 22. The syringe was placed into an automated pump that would push the syringe at a constant rate. An aluminum plate was placed 10 cm away from the needle. A 12kV voltage lead was clipped onto the needle and a ground wire was connected to the metal plate. The aluminum plate was covered with a white paper. The syringe was pushed at a rate of 0.005

ml/min. The chemical reaction of cobalt salt and acetic acid is shown in Eq. (1). The addition of water containing ethanol produces cobalt oxide and water (2).

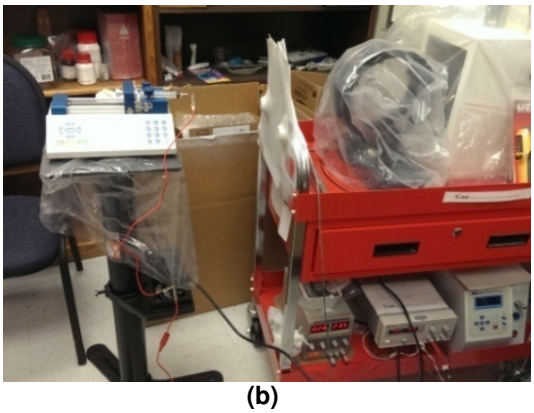
$$Co(Ac)_2 \cdot 4H_2O + C_2H_5OH \rightarrow CH_3COOC_2H_5 + Co^{2+} + OH^- \quad (1)$$

$$Co^{2+} + 2OH^- \rightarrow Co(OH)_2 \rightarrow CoO + H_2O \quad (2)$$

The nanofibers were made via electrospinning method. Fig. 1a shows the schematic of the electrospinning setup. A high voltage source is attached to the exiting needle gage. A ground is attached to a metal plate where the nanofiber products will settle. The voltage creates an electric field and attracts the compound solution to the settling plate. A mechanical plunger is squeezed to push the solution at a specified rate. The constant pressure to the flow allows consistency and accuracy to manifest nanofiber materials. Once the electric power was applied, the process started to build a fiber layer onto the plate. Fig. 1b shows the actual experimental instruments.



(a)



(b)

Fig. 1. Schematic and apparatus showing nanofiber manufacturing process: (a) Schematic of the electrospinning process, (b) Experimental instrumentation

The initial observation was that the needle produced multiple fibers at the exit. A modification may be made to use a smaller gage needle; this would reduce the number of fibers on the exit and have a better finish. There was much interference regarding the environment. There is draft created in the space for the electrospinning due to the air flow. There are electronic interferences observed as well. A well-insulated and vacuumed environment would yield better results in view of the uniform electrospinning.

2.3 Characterization of the Nanofibers

The electrospun nanofibers were observed by scanning electron microscopy. For hyperthermia tests, each of the nanofiber mats was cut into squares with the size of 100mm. Such specimens were settle down and secured onto a glass plate. For each hyperthermia test, the plate was placed into the microwave with a time increment of 5 seconds and up to maximum of 25 seconds. Each time, when the specimen was taken out of the microwave, the temperature was recorded with aninfraredthermometer. The thermometer was placed at a consistent distance of 10 cm away from the specimens. The temperature measurement location was randomly chosen on the material. For each test, at least five temperature readings were recorded in specified time interval.

3. RESULT AND DISCUSSION

The first batch of nanofibers included cobalt oxide without adding acetic acid and the second with the acetic acid addition. The third batch is an iron cobalt oxide. The fourth contains cobalt and titanium oxide. The fifth is an iron oxide specimen. The final batch is titanium cobalt oxide. For clarity, the following sample numbering system is used in this paper. Sample No. 1 is the PVP nanofiber mat containing CoO without (w/o) acetic acid. Sample No. 2 refers to the PVP nanofiber mat containing CoO with the addition of acetic acid. Sample No. 3 stands for the PVP nanofiber mat containing Fe_3O_4+CoO. Sample No. 4 is the PVP nanofiber mat containing uniformly distributed TiO_2 and CoO. Sample No. 5 is the PVP nanofiber mat containing Fe_3O_4. Sample No. 6 is the PVP nanofiber mat containing TiO_2 and CoO with the two oxides not uniformly distributed due to the magnets. There was a significant separation of oxides in the last batch when the magnetic field was added, which was generated by a pair of

Nd-Fe-B permanent magnets placed at the two side edges of the nanofiber receiving screen. The Co-containing compound did not spread out evenly. Instead, a Co-rich region and a Ti-rich region were found. Thus, No. 6 had a clear separation of cobalt from titanium due to the magnets that secured the plate. The element was attracted and shifted downward while the cobalt was lifted upwards. During the testing phase, the data were collected separately; one for Ti-oxide concentrated region and the other for Co-oxide concentrated region.

3.1 Morphology

The electrospun nanofibers were observed by scanning electron microscopy and typical images were recorded. Fig. 2(a) and 2(b) show the morphology of nanofibers containing CoO magnetic nanoparticles. We can see that the nanofibers were deposited on the substrate to form fiber mats. The average size of the nanofiber is about 500 nm as shown in Fig. 1a for the material without adding acetic acid during the processing, but the addition of acetic acid changed the morphology significantly. Some fibers crushed down into thin ribbons or films. The thin ribbons have the width of about 20 micrometer. The reason for the ribbon formation is due to the low viscosity of the solution. The acetic acid suppress the hydrolysis of the cobalt salt and prevent the formation of $Co(OH)_2$ formation. The low viscosity due to the existence of acetic acid could result to the collapse of the soft fibers along the thickness direction of the fiber mat. Combing of different fibers could also occur. Therefore, the image as shown in Fig. 2(b) was found.

Fig. 2(c) shows the morphology of the PVP nanofiber mat containing Fe_3O_4+CoO, the size of the fiber is the smallest one among the six specimens. In Fig. 2(d), the PVP nanofiber mat containing uniformly distributed TiO_2 and CoO is revealed. The fiber size increased a lot. The possible explanation is that the TiO_2 precursor has much high viscosity. Under the driving force of the high DC voltage, the shrinkage due to solvent evaporation is much less than other five cases.

Fig. 2 (e) is the SEM image of the PVP nanofiber mat containing Fe_3O_4. Fe_3O_4 tends to form clusters. Under the microscopic analysis, some nodes were observed, which is due to the Fe_3O_4 cluster formation. The last SEM image, Fig. 2(f), shows the PVP nanofiber mat containing TiO_2CoO with the two oxides not uniformly distributed due to the magnets. The fibers are finer than those shown in Fig. 4(d), which means the magnetic effect may cause the size deduction in the electrospinning process. But more studies are needed to confirm this.

3.2 Hyperthermia Behavior

Table 1 lists the temperature data for the iron oxide and cobalt oxide containing nanofiber mat. The specimen No. 3 with the composition of Fe_3O_4+CoO showed the fastest increasing in temperature under the exposure to the electromagnetic field.

In the Table, the temperature change of the pure iron oxide particles embedded in the PVP nanofibers (Sample No. 5) is shown. Comparing the results of the two nanomaterials, it is found that the temperature increases not so fast as in the case of Specimen No.3.

The human body core temperature is 37℃ and a severe fever is 38.9℃. From Fig. 3, the highest temperature reached was by the iron cobalt oxide nanofiber, which is 47.3℃ and the lowest one was by the iron oxide, 38.4℃. At the 25 second mark all of the substances reached over 38℃. The traditional cancer treatment temperature ranges from 41.5℃ to 45℃ in which the cancer cell could be severely injured or eliminated. Sample No. 2 and 5 did not reach the temperature high enough to be effective. The adhesive, PVP, used started to smoke and left a strong pungent smell. The adhesive must have burn during the latter phase of the heat. If it wasn't for the adhesive, the material could have stayed longer in the microwave. From Fig. 3 the upper bound was created by iron cobalt oxide and the lower bound from titanium concentrated titanium cobalt oxide.

Titanium cobalt oxide was studied with emphasis on titanium and cobalt. From Fig. 4, titanium cobalt oxide with cobalt abundance shows an increase of temperature at 25 seconds. Titanium enriched shows a lower amount of temperature rise. However the trend expects the element to converge to cobalt enriched composition. It is easily seen that Specimen No. 4 has more cobalt oxide clusters. Cobalt oxide creates higher temperatures and titanium oxide does not. Titanium oxide maybe used as a controlling component to regulate the temperature rise.

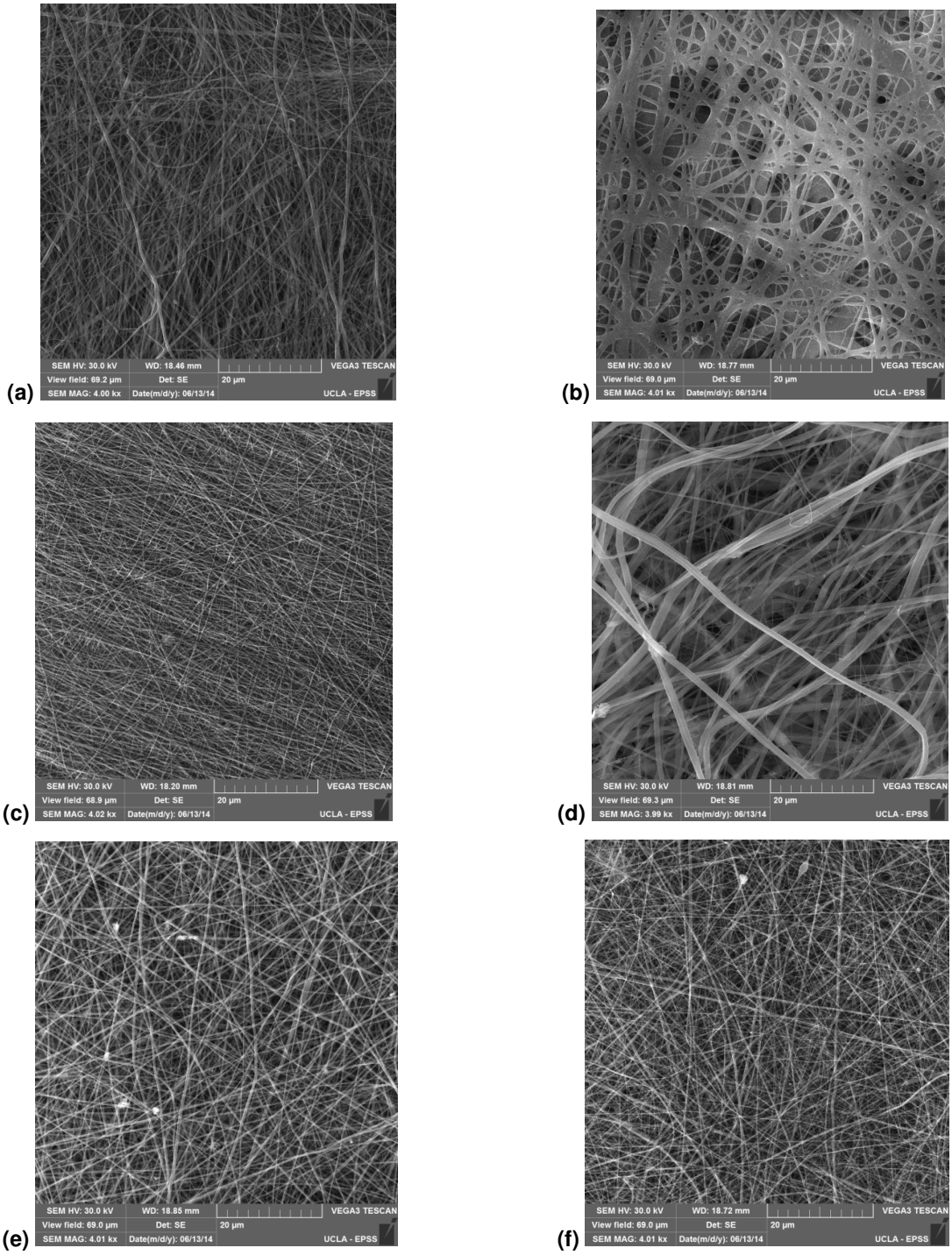


Fig. 2. Scanning electron microscopic analysis results of the electrospun fibers: (a) CoO-containing PVP fibers without adding acetic acid, (b) CoO-containing PVP fibers with addition of acetic acid, (c) The PVP nanofiber mat containing Fe_3O_4+CoO, (d) The PVP nanofiber mat containing uniformly distributed TiO_2CoO, (e) The PVP nanofiber mat containing Fe_3O_4, (f) The PVP nanofiber mat containing TiO_2CoO with the two oxides not uniformly distributed due to the magnets

Cobalt oxide with and without acetate addition during the electrospinning process were compared. The acid was an aqueous solution to help deliver the element into the syringe. From Fig. 5, up to 10 seconds the two does not have any differences. However, they do diverge and separate and by 25 seconds they are more than 5℃ apart. Cobalt with minimal acetate acid increased than the cobalt with acetate acid.

Table 1. Average temperatures in degree celsius of sample No. 3 (Fe_3O_4+CoO) and sample no. 5 (Fe_3O_4) with different time period exposures to the external electromagnetic field

Time (s)	0	5	10	15	20	25
Sample 3	23.9	30.1	31.5	38.5	42.7	47.3
Sample 5	23.9	27.4	31.2	34.4	34.6	38.4

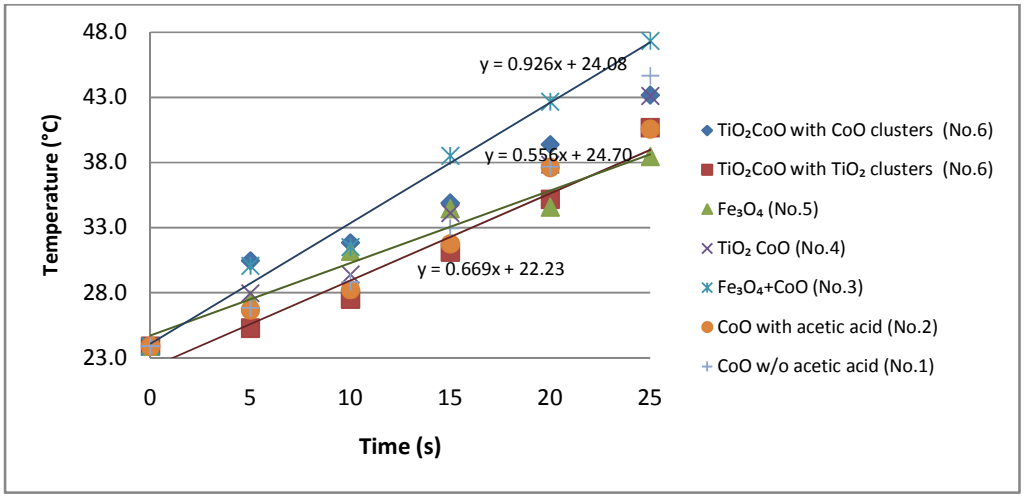


Fig. 3. Temperature changes of nanofibers with time via exposure to external field

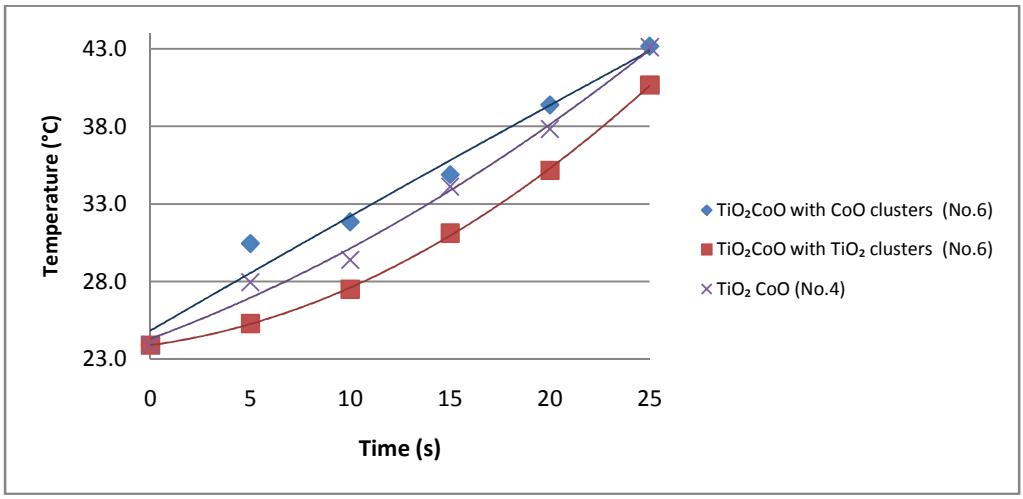


Fig. 4. Comparison between the titanium oxide concentrated region with the cobalt oxide concentrated region for the electrospun TiO_2CoO/PVP nanofiber mat specimen

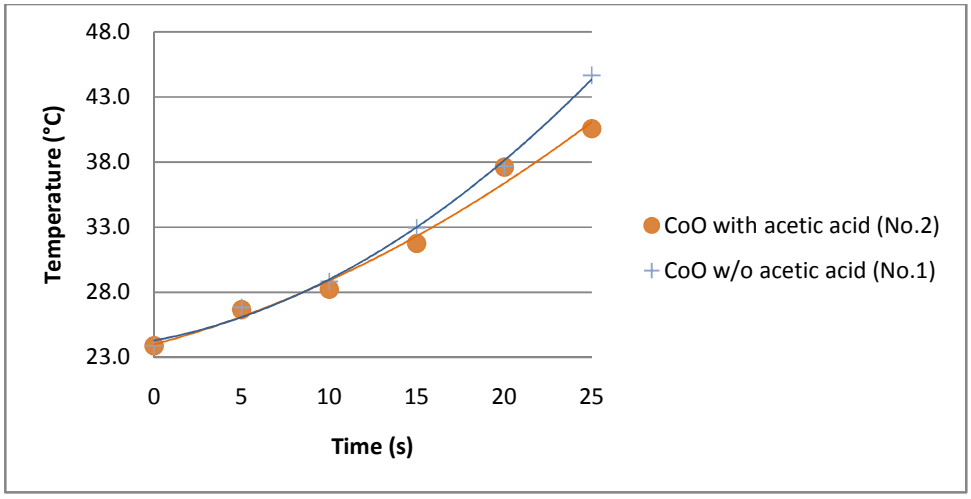


Fig. 5. Comparison between cobalt with and without acetic acid

4. CONCLUSIONS

Electrospinning can be used to make PVP nanofibers containing various oxide materials. The prepared nanofiber mats are responsive to the external electromagnetic field. The iron oxide-cobalt oxide containing nanofiber shows the fastest increasing in temperature among all the six materials. The lowest rising in the temperature is for the nanomaterial just containing pure iron oxide. Increase of cobalt oxide content also increases temperature in the titanium cobalt oxide mixture nanomaterial. Titanium dioxide, on the other hand, increases the temperature slower. This indicates that titanium oxide could be used to help regulate temperature. The temperature of the electrospun fiber with cobalt without acetate acid increased more than that of the electrospun fiber with cobalt with acetate acid.

CONSENT

All authors consent to publish the research results in this international journal.

ETHICAL APPROVAL

There is no ethical issue associated with the publication of this paper.

ACKNOWLEDGEMENT

This work is supported by the National Science Foundation (NSF) under Grant Number CMMI-1333044. YXG also acknowledges the support by the CAFA Faculty Development Grant and the Cal Poly Pomona 2013-2014 President's Research, Scholarship and Creative Activity Program Grant.The SEM in the University of California, Los Angeles(UCLA), Department of Earth, Planetary, and Space Sciences was funded through the Army Research Office's Defense University Research Instrumentation Program (DURIP). Theauthors acknowledge Professor Axel K. Schmitt and Rita Economos for access to the scanning electron microscope in the Department of Earth, Planetary, and Space Science at University of California, Los Angeles.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Wahyudiono S. Machmudah K. Murakami, S. Okubayashi M. Goto, Generation of PVP fibers by electrospinning in one-step process under high-pressure CO_2, International Journal of Industrial Chemistry. 2013;4:27.
2. Zhao Q, Huang Z, Wang C, Zhao Q, Sun H, Wang D. Preparation of PVP/MEH-PPV composite polymer fibers by electrospinning and study of their photoelectronic character, Materials Letters. 2007;61:2159-2163.
3. Bai J, Li Y, Li M, Wang S, Zhang C, Yang Q. Electrospinning method for the preparation of silver chloride nanoparticles

in PVP nanofiber, Applied Surface Science. 2008;254:4520-4523.
4. Enculescu M, Evanghelidis A, Enculescu I. Influence of morphology on the emissive properties of dye-doped PVP nanofibers produced by electrospinning. Journal of Physics and Chemistry of Solids. 2014;75:1365-1371.
5. Wang M, Fang D, Wang N, Jiang S, Nie J, Yu Q, Ma G. Preparation of PVDF/PVP core–shell nanofibers mats via homogeneous electrospinning, Polymer. 2014;55:2188-2196.
6. Rasekh M, Karavasili C, Soong YL, Bouropoulos N, Morris M, Armitage D, Li X, Fatouros DG, Ahmad Z. Electrospun PVP–indomethacin constituents for transdermal dressings and drug delivery devices, International Journal of Pharmaceutics. 2014;473:95-104.
7. He X, Arsat R, Sadek AZ, Wlodarski W, Kalantar-zadeh K, Li J. Electrospun PVP fibers and gas sensing properties of PVP/36° YX $LiTaO_3$ SAW device, Sensors and Actuators B: Chemical. 2010;145:674-679.
8. Maingon P, Nouhaud É, Mornex F, Créhange G. Stereotactic body radiation therapy for liver tumours, Cancer/Radiothérapie. 2014;18:313-319.
9. Greenhalgh TA, Symonds RP. Principles of chemotherapy and radiotherapy, Obstetrics, Gynaecology & Reproductive Medicine. 2014;24:259-265.
10. Corato RD, Espinosa A, Lartigue L, Tharaud M, Chat S, Pellegrino T, Ménager C, Gazeau F, Wilhelm C. Magnetic hyperthermia efficiency in the cellular environment for different nanoparticle designs, Biomaterials. 2014;35:6400-6411.
11. Garaio E, Collantes JM, Garcia JA, Plazaola F, Mornet S, Couillaud F, Sandre O, A wide-frequency range AC magnetometer to measure the specific absorption rate in nanoparticles for magnetic hyperthermia, Journal of Magnetism and Magnetic Materials. 2014;368:432-437.
12. Sadat ME, Patel R, Bud'ko SL, Ewing RC, Zhang J, Xu H, Mast DB, Shi D. Dipole-interaction mediated hyperthermia heating mechanism of nanostructured Fe_3O_4composites, Materials Letters. 2014;129:57–60.
13. Deatsch AE, Evans BA. Heating efficiency in magnetic nanoparticle hyperthermia, Journal of Magnetism and Magnetic Materials. 2014;354:163–172.
14. Kumar CSSR, Mohammad F. Magnetic nanomaterials for hyperthermia-based therapy and controlled drug delivery, Advanced Drug Delivery Reviews. 2011;63:789–808.
15. Laurent S, Dutz S, Häfeli UO, Mahmoudi M. Magnetic fluid hyperthermia: Focus on superparamagnetic iron oxide nanoparticles, Advances in Colloid and Interface Science. 2011;166:8–23.
16. Veverka M, Veverka P, Jirák Z, Kaman O, Knížek K, Maryško M, Pollert E, Závěta K. Synthesis and magnetic properties of $Co_{1-x}Zn_xFe_2O_{4+y}$ nanoparticles as materials for magnetic fluid hyperthermia. Journal of Magnetism and Magnetic Materials. 2010;322:2386-2389.
17. Tseng CL, Chang KC, Yeh MC, Yang KC, Tang TP, Lin FH. Development of a dual-functional Pt–Fe-HAP magnetic nanoparticles application for chemo-hyperthermia treatment of cancer, Ceramics International. 2014;40:5117-5127.
18. Duong E, Chan SY, Gan YX, Zhang L. Centrifugal deposition of iron oxide maganeticnanorods for hyperthermia application. Journal of Thermal Engineering. 2015;1:99-103.
19. Huang HS, Hainfeld JF, Intravenous magnetic nanoparticle cancer hyperthermia, International Journal of Nanomedicine. 2013;2521–2532.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=645&id=31&aid=6250