Asian Journal of Chemistry; Vol. 25, No. 11 (2013), 6413-6415

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2013.14992

Preparation of ZnO Microtube Capsule for Drug Delivery System *via* Microemulsion-Sol-Hydrothermal Method

Y. JI[1], H. ZHU[1], H.H. BAO[1], L. ZHANG[1], H.Z. YANG[2] and X.D. ZHANG[1,*]

[1]Department of Stomatology, General Hospital of Shenyang Military Area Command, Shenyang 110840, Liaoning Province, P.R. China
[2]Department of Biophysics, College of Basic Medical Science, China Medical University, Shenyang 110001, Liaoning Province, P.R. China

*Corresponding author: Tel./Fax: +86 24 83978251; E-mail: zyxdzhang@163.com

(*Received*: 18 December 2012; *Accepted*: 11 May 2013) AJC-13483

Cyclohexane, deionized water, CTAB and *n*-butyl alcohol were respectively adopted as oil phase, water phase, emulsifier and cosurfactant to prepare water-in-oil (w/o) emulsion. Zinc acetate dihydrate, monoethanolamine and ethanol was respectively adopted as reactor, complex agent and solvent to prepare the sol as the Zn source. Then the ZnO microtube capsule can be obtained through the hydrothermal route. X-ray diffraction and scanning electron microscope were chosen to investigate the crystallization properties and morphology of the sample. Results reveal that the hollow capsule with a few micrometers in size can be obtained through the combination of microemulsion-sol-hydrothermal method. Furthermore, a schematic model of the experiment is proposed.

Key Words: W/O, Microemulsion-sol-hydrothermal method, Microtube capsule.

INTRODUCTION

Capsule has received much attention in recent years due to its controllability in shape and size. Capsule is a kind of metallic, metalloid and organic enclave with a core-shell structure[1]. The micro/nano capsule, with the dimension scale from several nanometers to tens of micrometers, can encapsulate tiny drug molecules. In this way, the activity of the drugs can be enhanced and the rate of drug release is controllable by adjusting the dimension of the drugs and micro pore[2]. Furthermore, the micro/nano capsule for drugs is promising in drug targeting and controlled release owing to the versatility of shell materials and easily crossing blood brain barrier. Therefore, the investigation of micro/nano capsule as a kind of carrier for drug delivery system is a hot issue both in the field of material science and medical science.

Organic polymer used to be adopted as carriers in drug delivery system[3,4]. However, for most organic polymer, the mechanical strength, chemical stability and biocompatibility is poor, especially, some of polymer is toxic, which hindered the application of polymer shell *in vivo*. In contrast, inorganic material especially inorganic ceramic is considered as a promising candidate for medical capsule shell owing to its excellent mechanical and biological properties[5]. Silica and zinc oxide inorganic ceramics are considered as desirable capsule shells owing to their favourable mechanical stability, chemical stability and biocompatibility[6-12]. In our previous study, silica hollow capsules were prepared *via* water-in-oil (w/o) emulsion method[13]. However, shapes of the capsules are difficult to control owing to the instability of emulsion. In contrast, ZnO is versatile in shape controllability[14], making it superior in preparation of capsule shells. To date, ZnO hollow capsules has been prepared by various wet-chemical methods such as sol-gel, microemulsion and hydrothermal method[15]. For sol-gel method and microemulsion method, the shape and size of hollow capsule is difficult to control rigorously owing to the relative high sintering temperature. For hydrothermal method, reacting solution is sealed in a high pressure reaction kettle and the shape and size of capsules could be controlled owing to the relative low reaction temperature. In this case, the stability of reacting solution plays an important role in preparing the hollow capsule.

In this paper, mixture of w/o emulsion and $Zn(OH)_2$ sol was adopted as reacting solution of hydrothermal method and a microemulsion-sol-hydrothermal method was devised to prepare the ZnO hollow capsule. Furthermore, the formation mechanism of the system is investigated, which pave the way for the application of ZnO as medical capsule shell.

EXPERIMENTAL

All of the reagent used in the experiment are chemical pure. A microemulsion-sol-hydrothermal method was adopted to prepare the ZnO powder.

0.9773 g of monoethanolamine (MEA) was dissolved in 20mL ethanol, then 3.112 g $Zn(CH_3COO)_2{\cdot}2H_2O$ was added into the solution in the molar ratio of Zn^{2+} : MEA = 1 : 1. A transparent sol can be formed after magnetic stirring for *ca.* 0.5 h; 1 g $C_{19}H_{42}NBr$ (CTAB) was added into 30 mL cyclohexane, followed by the dropwise addition of 1.8 mL *n*-butyl alcohol. Afterwards, 1.8 mL deionized water was dropped into the solution slowly. After magnetic stirring for a while, a transparent emulsion can be formed; 0.15 mL $Zn(OH)_2$ sol was dropped into the emulsion slowly and a transparent precursor reacting solution can be obtained after magnetic stirring for *ca.* 20 min. The precursor reacting solution was dispersed by the ultrasonic for *ca.* 10 min, followed by sealed into a Teflon kettle for hydrothermal treatment. After treated at 120 ºC for 2 h, the product was separated by centrifugation and washed ultrasonically in ethanol and acetone for 3 times, respectively. Then, the product was dried at room temperature to obtain the ZnO powder. The flow chart of experiment is shown in Fig. 1.

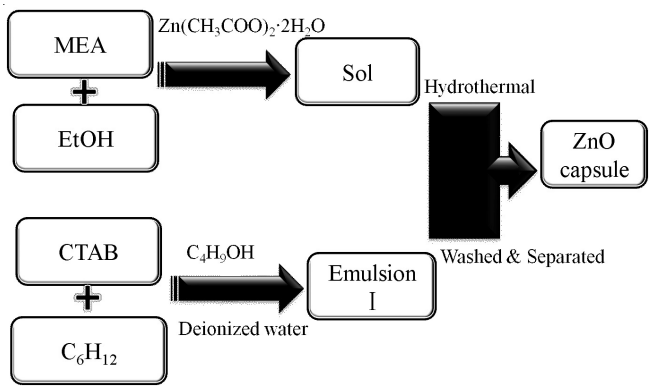

Fig. 1. Flow chart of the experiment

Detection method: SEM (Shimadzu SSX-550) was adopted to observe the morphology of the ZnO powder; XRD (D/max 3A, Rigaku) was adopted to investigate the crystallinity of sample.

RESULTS AND DISCUSSION

Fig. 2 shows XRD pattern of ZnO powder prepared by the microemulsion-sol-hydrothermal method. A sharp diffraction peak can be found at about $2\theta = 32^{\circ}$, which can be attributed ZnO crystals according to the standard JCPDS data (No. 36-1451). It is interesting that there is no diffraction peak of other impurities or other orientation of ZnO crystal, *i.e.*, ZnO crystal in the experiment has a single orientation. Therefore, it is speculated that ZnO powder derived from the microemulsion-sol-hydrothermal process has a unique crystal structure

Morphology of powders is shown in Fig. 3. Fig. 3(a) and Fig. 3(b) are the local amplicaiton images. It is shown that ZnO microtubes can be obtained derived from microemulsion-sol-hydrothermal method. From Fig. 3(a), the ZnO microtubes have a uniform size in length; from Fig. 3(b), the ZnO microtubes possess a dumbbell structure, the length and diameter of the microtube is about 7 μm and 1.5 μm, respectively. Therefore, the ZnO sample can be applied as the capsule for drug delivery system and the work of drug loading experiment is in progress.

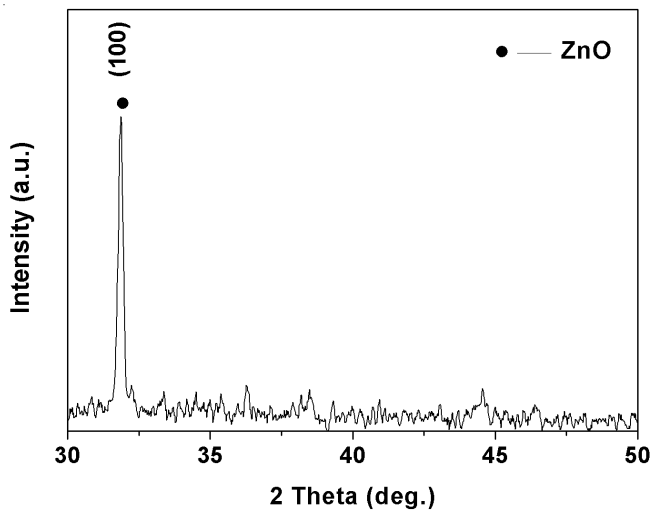

Fig. 2. XRD pattern of ZnO sample prepared by the microemulsion-sol-hydrothermal method

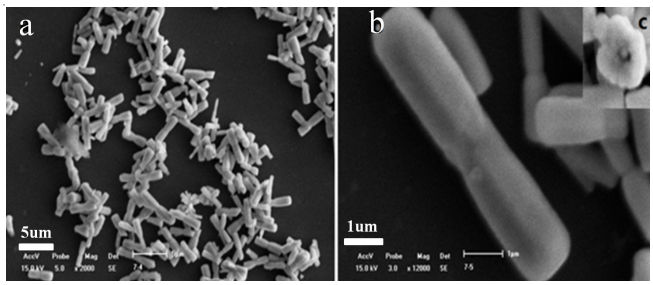

Fig. 3. SEM images of the ZnO sample. (a) and (b) are the local amplicaiton images

Mechanism model of the reacting solution formation is proposed according to the experimental results (Fig. 4). In the experiment, CTAB and *n*-butyl alcohol is the surfactant and cosurfactant, respectively. At first, monolayer surfactant aggregate at the interface of water and oil (Fig. 4a); when there is other surfactant molecular in the emulsion, hydrophobic group impels the surfactant molecular escape from water phase. As a result, the molecular will auto aggregate to form micelles in the emulsion (Fig. 4b); when the Zn containing sol was added into the emulsion, the sol tends to aggregate at the interface of micelles due to amphipathy of the sol. As a result, the unique structure of reacting solution is obtained (Fig. 4c). Since monoethanolamine is alkaline, the Zn containing sol is considered as $Zn(OH)_2$ sol. The formation of the $Zn(OH)_2$ sol can be expressed in eqn. (1). Then, ZnO crystal can be obtained during the hydrothermal process, which can be expressed in eqn. (2).

$$Zn^{2+} + 2OH^{-} \leftrightarrow Zn(OH)_2 \quad (1)$$

$$Zn(OH)_2 \leftrightarrow ZnO + H_2O \quad (2)$$

Since the $Zn(OH)_2$ sol tends to aggregate at the interface of micelles, the shape of ZnO powder is decided by the shape of micelles template. As a result, ZnO hollow microtube can be obtained, which can be applied as capsules for water-soluble

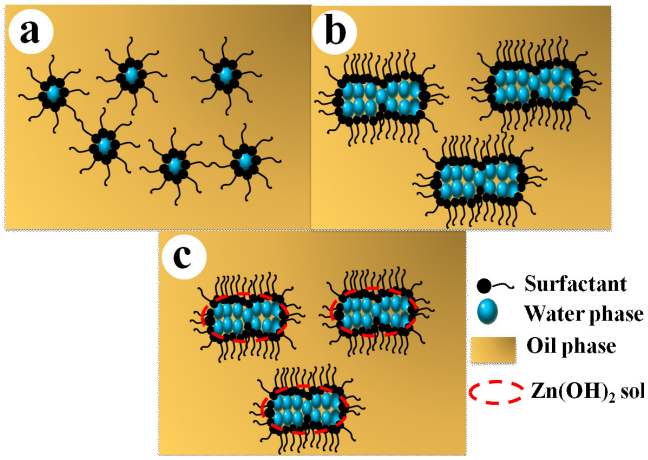

Fig. 4. Schematic formation process for reacting solution

drugs. The relative work on encapsulation of drug is in progress.

Conclusion

Novel microemulsion-sol-hydrothermal method was adopted to prepare hollow ZnO hollow microtube as capsule shell. Micelles in the microemulsion are work as template and microscopic shape of the ZnO capsule is decided by shape of micelles.

ACKNOWLEDGEMENTS

The author acknowledged the aid and instruction of Prof. Y. Qi, Northeastern University, P.R. China.

REFERENCES

1. G.R. Duan, A.M. Li, X.J. Yang, L.D. Lu and X. Wang, *Micropor. Mesopor. Mater.*, **116**, 86 (2008).
2. W. Zeng, X.F. Qian, Y.B. Zhang, J. Yin and Z.K. Zhu, *Mater. Res. Bull.*, **40**, 766 (2005).
3. M.S. Romero-Cano and B. Vincent, *J. Control. Release*, **82**, 127 (2002).
4. M. Changez, K. Burugapalli, V. Koul and V. Choudhary, *Biomaterials*, **24**, 527 (2003).
5. S.-J. Choi, J.-M. OH and J.-H. Choy, *J. Ceram. Soc. Jpn.*, **117**, 543 (2009).
6. Z.Z. Li, S.A. Xu, L.X. Wen, F. Liu, A.Q. Liu, Q. Wang, H.Y. Sun, W. Yu and J.F. Chen, *J. Control. Release*, **111**, 81 (2006).
7. J.F. Chen, H.M. Ding, J.X. Wang and L. Shao, *Biomaterials*, **25**, 723 (2004).
8. C. Yagüe, M. Moros, V. Grazú, M. Arruebo and J. Santanaria, *Chem. Eng. J.*, **137**, 45 (2008).
9. Y.F. Zhu, J.L. Shi, W.H. Shen, X.P. Dong, J.W. Feng, M.L. Ruan and Y.S. Li, *Angew. Chem. Int. Ed.*, **44**, 5083 (2005).
10. N.J. Einerson, K.R. Stevens and W.J. Kao, *Biomaterials*, **24**, 509 (2003).
11. Q. Yuan, S. Hein and R.D.K. Misra, *Acta Biomater.*, **6**, 2732 (2010).
12. F. Muhammad, M.Y. Guo, Y.J. Guo, W.X. Qi, F.Y. Qu, F.X. Sun, H.J. Zhao and H.J. Zhu, *J. Mater. Chem.*, **21**, 13406 (2011).
13. H.Z. Yang, Y. Ji, X.M. Yu, H. Zhu and L. Zhou, *Asian J. Chem.*, **24**, 3507 (2012).
14. C.T. Lee, *Materials*, **3**, 2218 (2010).
15. Q.P. Luo, B.X. Lei, X.Y. Yu, D.B. Kuang and C.Y. Su, *J. Mater. Chem.*, **21**, 8709 (2011).