KnE Energy & Physics

PhysBioSymp17
The 2nd International Symposium on
Physics, Engineering and Technologies for Biomedicine
Volume 2018

Knowledge E
Engaging minds

Conference Paper

Two-stage ZnS Shell Coating on the CuInS2 Quantum Dots for Their Effective Solubilization

Vokhmintcev K.V.[1], Linkov P.A.[1], Samokhvalov P.S.[1], and Nabiev I.R.[1,2]

[1]National Research Nuclear University MEPhI (Moscow Engineering Physics Institute), Kashirskoe shosse 31, Moscow, 115409, Russia
[2]Laboratoire de Recherche en Nanosciences, LRN-EA4682, Université de Reims Champagne-Ardenne, 51100 Reims, France

Abstract

High-precision diagnostics is one of the necessary conditions for effective treatment of diseases. Bioimaging is one of the most promising modern methods of tumor diagnosis. High-quality luminophores are necessary for effective bio-imaging. $CuInS_2$(CIS) quantum dots (QDs) are very promising luminophores for these applications due to their low toxicity and long-term stability of their properties. Two batches of CIS QDs with different positions of the luminescence maximum have been obtained. The position of the luminescence maximum can be controlled by changing the Cu to In ratio; a decrease in this ratio cause a blue shift of the luminescence.

The standard procedure of CIS synthesis yields QDs covered with thiols, which form strong bonds with the surface and prevent the ligand exchange; hence, it is very hard to adapt CIS QDs for biological tasks using the standard hydrophobic to hydrophilic ligand exchange procedure. We have developed a two-stage shell coating procedure yielding CIS QDs covered with amines, which is suitable for ligand exchange; hence, the resultant QDs can be adapted for modern biological and medical applications.

Keywords: Quantum dots, $CuInS_2$, solubilization,

Corresponding Author:
Vokhmintcev K.V.
VoKirill@gmail.com

Received: 17 January 2018
Accepted: 25 March 2018
Published: 17 April 2018

Publishing services provided by Knowledge E

Selection and Peer-review under the responsibility of the PhysBioSymp17 Conference Committee.

1. Introduction

Bioimaging is a very useful modern method for disease diagnosis and investigation of biological processes [1, 2]. The main goal that has to be achieved for an effective bioimaging is the use of a highly luminescent phosphor with long-term stability of properties under different conditions, as well as with the minimum possible toxicity. The most promising luminophores for this application are quantum dots (QDs). The use of QDs for bioimaging has significantly improved its capacity. Compared to the previous

generation of luminophores, organic dyes, QDs have superior properties, such as size-tunable fluorescence, a unique flexibility of the excitation wavelength, a high fluorescence quantum yield, and large two-photon absorption cross-sections [3]. The most popular types of QDs are based on CdSe and, hence, have a significant disadvantage in terms of biomedical applications, because cadmium is toxic and its presence precludes the applicability of CdSe QDs in vivo.

In this study, we have synthesized nontoxic cadmium-free $CuInS_2$/ZnS QDs (CIS QDs) and developed a two-stage coating procedure for adaptation of these QDs for biological applications. QD adaptation to biological procedures means the transfer of the QDs from organic to water phase by exchanging hydrophobic ligands to hydrophilic ones. The necessity of a two-stage coating procedure is determined by the fact that, after the first stage, the QDs are coated with thiol ligands, which are strongly bound to the surface, thereby preventing the replacement of ligands. After the second stage of coating in an excess of amines, the surface of the QDs is coated with amines, which are much easier to replace with other ligands.

2. Materials and methods

$CuInS_2$ QD cores were synthesized by the heat-up method. QDs with luminescence in the near-IR region were synthesized as following: copper iodide (I) (99.999%) (1 mmol) and indium acetate (99.99%) (1 mmol) were mixed with 5 ml of dodecanthiol (98%) (DDT) in a 25-ml three-necked round-bottom flask. The flask was heated to 120°C and evacuated at 10 mbar until a clear solution formed. The reaction mixture was rapidly heated to 230°C and kept at that temperature for 15 min in an argon atmosphere. QDs with luminescence in the visible region were synthesized according to the same procedure except that the amounts of copper iodide (I) and indium acetate were 0.167 and 1 mmol, respectively. Then, the synthesized QDs were purified by two precipitation/dissolution cycles, with methyl acetate (99%) and toluene serving as the precipitator and the solvent, respectively. The purified solution of QDs in toluene was mixed with 5 ml of DDT; then, toluene was removed from the mixture under vacuum.

The ZnS shell was formed in two steps. The zinc precursor was the same at both steps and was prepared according to the following procedure. Zinc oxide (30 mmol), 2-ethylhexanoic acid (61.5 mmol) (99%), and 40 ml of ODE were mixed, the reaction mixture was heated to 120°C and kept until clear solution formed under continuous stirring. The sulfur precursor for the first shell formation step was prepared by dissolution of S powder in trioctylphosphine (97%) and 0.5 ml of ODE under an argon flow at

150°C. The sulfur precursor for the second step was prepared by dissolving 34 mmol of thiourea (99%) in 40 ml of triethyleneglycol dimethylether (98%) under sonication.

The first ZnS shell layering procedure was carried out as follows. A solution of QDs in DDT was mixed with 1-octadecen (99%) (ODE) in a 100-ml three-necked round-bottom flask. The reaction mixture was degassed under vacuum at 100°C during 25 min; then, the flask was heated to 210°C. Solutions of precursors containing 3 mmol of the target substance were introduced into the solution within 30 min using syringe pumps. The resulting solution was purified using a procedure similar to that used for the cores.

The second ZnS shell layer was applied using the following procedure. A QD solution in toluene was mixed with 12 ml of ODE and 12 ml of oleylamine (97%), and then toluene was removed from the solution in a rotary evaporator. The reaction mixture was transferred to a three-neck round-bottom flask and kept under vacuum at 100°C for 25 min. Then, 5 mmol of the zinc precursor and 5 mmol of the sulfur precursor were added dropwise to the solution at 180°C within 1 h. The QDs were purified using a procedure similar to that used for the cores.

The QDs were solubilized by the following procedure. A portion of the QD solution was purified twice using methyl acetate and hexane as the precipitant and the solvent, respectively. After the second precipitation, the QDs were dissolved in 0.8 ml of chloroform, 0.2 ml of a 15-mg/ml cysteine hydrochloride (98%) solution in methanol was added, and the mixture was stirred for 5 min. In order to remove unbound cysteine hydrochloride, 1 ml of methanol was added, the solution was centrifuged, and then the supernatant was decanted. This procedure was repeated twice. After the second decantation, the precipitate was dissolved in 0.65 ml of a 0.01 M aqueous solution of NaOH (98%). All reagents were purchased from Sigma-Aldrich.

3. Results and Discussions

Two types of $CuInS_2$/ZnS QDs with different Cu to In ratios (1:1 and 1:6) were synthesized. Their luminescence and absorption spectra are shown in Figure 1.

When the Cu to In ratio changes from 1:1 to 1:6, the absorption spectra change slightly, the exciton peak becomes more pronounced, but there is a significant blue shift of the luminescence maximum, from 711 to 606 nm. The valence band maximum of CIS QDs is composed of hybrid orbitals of S and Cu [*3*]; hence, a decrease in the proportion of copper in the QDs leads to a decrease in the copper contribution to the formation of the valence band maximum. This leads to a decrease in the valence band maximum level, and the band gap becomes wider.

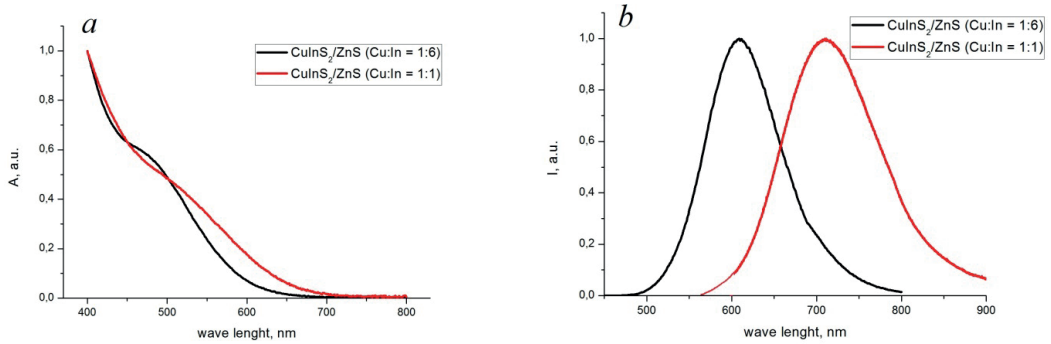

Figure 1: The (*a*) absorption and (*b*) luminescence spectra of CIS QDs with Cu to In ratios of 1:1 and 1:6.

In order to make the QDs synthesized in an organic medium compatible with biological fluids and tissues, it is necessary to convert their hydrophobic ligand shell into a hydrophilic one. This can be done by means of the solubilization procedure, a process of replacing hydrophobic ligands with hydrophilic cysteine or similar bifunctional thiol compounds.

Before solubilization, we had to obtain QDs coated with ligands which form weak bonds with the QD surface, since this simplifies the ligand exchange during the solubilization and increases its efficiency. Amines are the most common class of ligands which meet this requirement, forming a weak complex bond with the QD surface. Earlier, we demonstrated successful in amine capped solubilization of CdSe/ZnS QDs [4], but this method is unsuitable for CIS QDs, because their surface is covered with thiol ligands, and the formation of a strong covalent bond between the thiol molecule and the QD surface prevents efficient solubilization. Thiol–amine ligand exchange cannot be carried out directly on the CIS cores due to the low thermal stability of the cores, CIS decomposition starting at a lower temperature than the dissociation of thiol molecules from the CIS QD surface. The standard procedure for increasing the QD thermal stability is the formation of a ZnS shell. The previously developed ZnS coating technique in an amine media is not suitable in this case because of the CIS thermal instability. In order to overcome this problem, the two-stage shell coating method was developed. After the first shell coating, the thermal stability is increased, but the QD surface is still covered with thiols. The increased thermal stability allows shell formation in the amine media; this procedure is accompanied by thiol–amine ligand exchange, yielding in QDs prepared for solubilization.

In order to demonstrate that the method of $CuInS_2$/ZnS synthesis developed significantly improves the suitability of QDs for biological and medical applications, we tried to solubilize two batches of QDs, after the first and second steps of the shell formation.

The QDs with shells obtained by the two-step procedure were solubilized successfully; the mean hydrodynamic size of the QDs was 12 and 18 nm for QDs with Cu to In ratios of 1:6 and 1:1, respectively. The size distribution of the solubilized QDs is shown in Figure 2*a*. In contrast to the two-step coating, the one-step procedure failed to result in QD solubilization (Figure 2*b*). These results show that the two-step-coating method causes the formation of an amine ligand layer on the QD surface, which allows efficient ligand exchange during the solubilization; in contrast, one-step-coated QDs are thiol-capped, and the strong covalent bond between the QDs and the ligand molecules prevents solubilization.

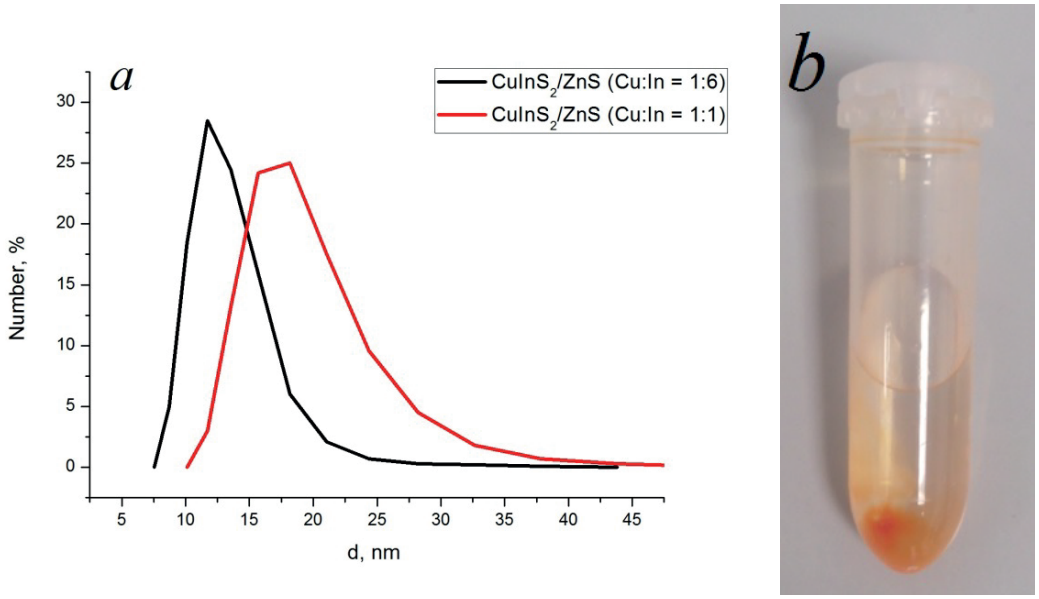

Figure 2: (*a*) Size distribution of the solubilized QDs obtained by the new two-step shell formation method. (*b*) The precipitate of the QDs obtained by the one-step shell formation method after unsuccessful solubilization.

4. Conclusions

Cadmium-free $CuInS_2$ QDs have been synthesized by the heat-up method. The position of the luminescence maximum was controlled by changing the Cu to In ratio. A decrease in the Cu to In ratio from 1:6 to 1:1 leads to a shift of the luminescence maximum of $CuInS_2$/ZnS QDs from 711 to 606 nm. This effect is due to a decrease in copper orbital contribution to the formation of the valence band maximum, which leads to its decrease and, hence, an increase in the band gap. The two-step shell layering method has been developed for adaption of the CIS QDs to biological applications. It has been established that the method developed allows obtaining QDs covered

with amine ligands and, hence, effectively transferring the QDs to the aqueous media by exchanging hydrophobic ligands to hydrophilic ones. In contrast to the method developed, the standard procedure of CIS synthesis leads to the formation of QDs coated with thiol ligands, the strong covalent bond between the QD surface and thiol molecules preventing effective ligand exchange and decreasing the suitability of CIS QDs for biological and medical applications.

Acknowledgments

This study was supported by the Ministry of Education and Science of the Russian Federation, State Contract no. 16.1034.2017/PCh.

References

[1] W. – C. Wu, C.-Y. Chen, Y. Tian, S.- H. Jang, Y. Hong, Y. Liu, R.Hu, B. Zhong Tang, Y.-T. Lee, C.-T. Chen, W.- C. Chen, A. K.-Y. Jen, "Enhancement of Aggregation-Induced Emission in Dye-Encapsulating Polymeric Micelles for Bioimaging", Advanced Functional materials, vol. 20, pp. 1413-1423, 2010.

[2] I. C. Kwon, C.-H. Ahn, S. Y. Park, "Dye-Condensed Biopolymeric Hybrids: Chromophoric Aggregation and Self-Assembly toward Fluorescent Bionanoparticles for Near Infrared Bioimaging",Chemistry of materials, vol 21, pp 5819-5825, 2009.

[3] M. Uehara, K. Watanabe, Y. Tajiri, H. Nakamura, H. Maeda, "Synthesis of $CuInS_2$ fluorescent nanocrystals and enhancement of fluorescence by controlling crystal defect", The Journal of Chemical Physics, 129, 134709, 2008.

[4] A. Sukhanova, K. Even-Desrumeaux, P. Chames, D. Baty, M. Artemyev, V. Oleinikov, I. Nabiev, "Engineering of ultra-small diagnostic nanoprobes through oriented conjugation of single-domain antibodies and quantum dots", Protocol exchange, 2012.