International Journal of Engineering

Journal Homepage: www.ije.ir

Nanotechnology and Neuroscience Convergence: A Novel Tool for Neurotransmitters Monitoring

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PAPER INFO

Paper history:
Received 02 November 2016
Received in revised form 09 January 2017
Accepted 09 February 2017

Keywords:
Neurotransmitter
Synaptic Transmission
Bioconjugating
Bioimaging
$CuInS_2$ Quantum Dots
Photo-luminescence

ABSTRACT

Since neurotransmitters significantly influence the brain activity, our understanding of the human brain will remain imperfect until all aspects relating to them become clear. One of the key challenges in neuroscience researches and therapies is elucidating the mechanisms by which the neurotransmitter release take place and is regulated in quantity and in time. Despite the enormous number of studies carried out to illuminate this function, efficient methods for momentary detection and visualizing these tiny neurochemicals have not been developed yet. Recent advances in nanomaterials have launched a new class of fluorescent labels by conjugating quantum dots (QDs) with biomolecules. Cadmium-based QDs have been by far the most developed in bioimaging; however, their doubtful future owing to high toxicity has turned researchers' attention to more recently ternary nontoxic compounds, $CuInS_2$. In this article a novel application of $CuInS_2$ nanoparticles in neuroscience has been proposed. Accordingly, a newly developed synthesis method have been exploited applying refluxed procedure. The structure and surface analysis taken by TEM and FTIR analyses showed that the resulting nanocrystals have sizes ranging from 1.6 to 3.2 nm while their surface is functionalized with MPA capping ligands. Optical properties of $CuInS_2$, demonstrating broad absorption and narrow emission spectra, 250 nm and 150 nm, respectively, with PL peak of 656 nm and FWHM 49 nm, have also been revealed by spectroscopy. All confirm that QDs are very appropriate for neurotransmitter detection in a small synaptic cleft. It is also suggested that the minimum concentration of [Cu]/[MPA] required for complete surface coverage is 1:11.

***doi**: 10.5829/idosi.ije.2017.30.02b.01*

1. INTRODUCTION

The process of information flow between neurons is termed synaptic transmission. This highly regulated phenomenon in its most basic form is characterized by unidirectional communication from the presynaptic to postsynaptic neuron by the release of chemical neurotransmitters into the synaptic cleft or the synaptic gap, involving numerous biochemical reactions [1, 2]. The released neurotransmitters diffuse across the cleft, and four possible actions may happen to them: 1- binding to and activating the direct or indirect appropriate postsynaptic receptors, 2- endocytosis, 3- carried away by the blood stream, 4- enzymatic degradation [3-6]. Neurotransmitters play a major role in everyday life and functioning. The understanding of the fundamental mechanisms of neurotransmitter release and the development of methods to measure the amount of released neurotransmitter is crucial for insight into a better understanding of many aspects of neurotransmission [3, 4] including neural circuitry, the mechanisms of short-term plasticity [7], diagnosis of large number of pathologies associated with the reasons causing abnormalities stem from dysfunction of receptors and ion channels [8], a precursor/enzyme needed for biosynthesis, packaging, axoplasmic transport, exocytosis, active zones, postsynaptic receptors [5, 6], and ultimately treating the diseases related to such as Parkinson [9-12].

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Please cite this article as: M. Mirzaie, M. Jahanshahi, R. Khanbabaie, G. Najafpour Darzi, Nanotechnology and Neuroscience Convergence: A Novel Tool for Neurotransmitters Monitoring, International Journal of Engineering (IJE), TRANSACTIONS B: Applications Vol. 30, No. 2, (February 2017) 152-161

Detection, mapping and measurement of neurotransmitters are fraught with difficulty related to the complex and delicate brain tissues, requirements for stable measurements with high selectivity, temporal and spatial resolution, and data interpretations [12, 13]; moreover, understanding the communication via neurotransmitters is also a complicated concept remaining uninvestigated as it occurs in several forms. At least five types of neurotransmitter release or secretory pathways (usually operates simultaneously) can be defined in neurons. To add to the complexity of these parallel signaling pathways, scientists do not know exactly how many neurotransmitters exist [14]. Furthermore, neurotransmitter release is not assured in response to synaptic stimulation; rather, the process of vesicle fusion for individual release-competent vesicles is probabilistic, highly dynamic; it incorporates several forms of short-term plasticity [15].

According to the importance of these facts, a lot of efforts have been done by scientists to clear the neurotransmitter release machinery as well as to measure their amount *in vivo* in the brain; results in employing some methods for detecting and quantifying neurotransmitters (see Table 1) each with their own particular advantages and disadvantages [15].

To date, no single technique is universally suited to all contexts of neurotransmitter-release quantification and detection due to some disadvantages such as [16] complexity, being time-consuming, not easily adaptable for real-time [11] and in-situ monitoring (insufficient deep-brain optical access) [14], great challengeable detection for low neurotransmitter concentration, low sensitivity and selectivity, high cost [10], indirect and nonlinear neurotransmitter release reporter [3, 15], inability to distinguish which neurotransmitters have contributed and how much percentage to the measured results [17], requiring expensive and sophisticated instrumentation or complicated sample preparation and bulk-average-based method analyzing tools [18].

In recent years, neuroimaging is the least invasive means to measure neurotransmitter release [15] owing to its operational simplicity, high sensitivity, clinical safety, being relatively inexpensive [19] and real-time monitoring in three dimensions with millimeter spatial and temporal resolution in seconds to minutes over a large area (e.g., the whole brain) [20]. This method takes advantage of styryl dyes and organic fluorophores with the ability to selectively bind to a particular biomolecule [3, 19], but still presents numerous disadvantages, including the autofluorescence from tissue organic components during signal acquisition and the deep tissue imaging difficulty. A comparison between QDs and organic fluorophores is presented in Table 2 [19, 21, 22].

TABLE 1. Tools and methods for the detection or quantification of neurotransmitters

Tool / Method	Application(s)	Reference(s)
Radiolabeled methods:		
Radiolabeled neurotransmitters	Dopamine (DA)	[15]
Electrophysiological methods:		
Patch-clamp capacitance	ACh, GABA	[23-25]
Electrophysiological biosensors (sniffer patch)	Neurosecretion	[15]
Current-clamp postsynaptic potentials	Neurosecretion	[26]
Electrochemical methods:		
Amperometry	Serotonin (5-HT)	[27]
Fast-scan cyclic voltammetry	DA, 5-HT	[7, 28]
Carbon-fibre electrode voltammetry	Catecholamines, DA	[29]
Glassy carbon electrodes and differential pulse voltammetry	DA, 5-HT Epinephrine, Norepinephrine (NE)	[18]
High-speed chronoamperometry	DA	[30]
Optical methods: Fluorescent styryl dyes	DA	[15]
SynaptopHlourins	GABA	[17]
Total internal reflection fluorescence (TIRF)		[31]
single-molecule Förster resonance energy transfer (smFRET)	DA	[31]
Two-photon laser scanning microscopy (TPLSM)	neurotransmitter receptor, Glutamate (Glu)	[32]
Confocal laser scanning microscopy	GABA	[24]
Sampling methods:		
Push-pull perfusion sampling	Endomorphin, Glu	[6, 12]
Microdialysis	ACh, DA, NE, GABA, Aspartate, Taurine,Tyrosine (Tyr), 5-HT	[12, 28, 33]
Analytical techniques coupled to sampling methods:		
Capillary electrophoresis (CE)	GABA, DA	[6, 12]
Mass spectrometry (MS)	GABA, Ach	[34]
Thin-layer chromatography (TLC), HPLC, open tubular liquid chromatography (OTLC)	DA, Adrenaline, Noradrenaline, 5-HT, Tyr, Tryptophan	
Enzyme assays *imaging methods:*	Glu, ACh	[12]
Positron emission tomography (PET)	DA	[13, 15, 35]
Magnetic resonance imaging (MRI)		[15, 36]

TABLE 2. Comparison between QDs and organic fluorophores

	Quantum dots	Organic fluorophores	Reference(s)
Excitation	Very broad, UV lights can excite a QD of any size	Narrow excitation spectra	[37]
Emission band width	20-40 nm	50-100 nm	[21]
Fluorescence lifetime	10-40 ns	Few nanoseconds	[38]
Photostability (upon constant illumination with a 50 mW, 488 nm laser)	Stable for 14 h, resistant to photobleaching	Photobleaches completely in under 20 min	
Cell autofluorescence (reduces detection sensitivity)	None	Signals from the labeled molecules can be obscured by the cell autofluorescence	[21, 39]
Molar extinction coefficient	Approximately 105-106 M-1cm-1 (for CdSe QDs)	10-100 times smaller that of CdSe QDs	[21]
Brightness	More	Less	[9]
Range of emission colors	Wide	Narrow	[9]

To overcome the shortcoming of the previous methods, nanotechnology opens up entirely new avenues for the application of nanoscale materials with typical diameters ranging from 1 to 10 nm which well suited for visualizing and tracking biomolecules [36]. It uses standard fluorescence microscopy avoiding most of the inherent problems encountered in classical optical systems [19]. Semiconductor nanocrystals also known as quantum dots (QDs); composed of a heavy-metal core such as CdSe and usually a shell, provide an excellent illustration of this concept [19]. Due to their quantum confinement, QDs show unique and fascinating optical properties [40] such as readily excitability, broad absorption and size-tunable [21], narrow symmetric emission spectra [22] which render them ideal fluorophores for ultrasensitive, multicolor, and multiplexing applications in molecular biotechnology and bioengineering [22]; amenable for simultaneous detection of multiple targets. The large surface area of QDs coupled with a versatile surface chemistry provides a platform for bioconjugation [37, 39] which enables a multi-functional surface to be tailored to incorporate, for example, both diagnostic and therapeutic qualities [19]. They also display minimal photobleaching allowing molecular tracking over prolonged periods; thereby neuroscience-specific applications of QDs are starting to emerge. Numerous groups have demonstrated the practicality of QDs for both *in vitro* and *in vivo* bioimaging studies [39]. Table 3 shows the examples of the application of QDs in bioimaging.

TABLE 3. Examples demonstrating the application of QDs in bioimaging

QD	Bioimaging	Reference(s)
CdSe/ZnS core-shell, Cd/Te	*In vivo* imaging of prostate and lung tumor in mouse	[38]
CdSe/ZnS core-shell	*In vivo* targeted imaging and therapeutic modalities of breast cancer	[41]
CdSe/ZnS core-shell	*In vivo* targeted imaging of neck cancer; tumor cells in Hodgkin's lymphoma	[42]
CdSe/ZnS core-shell	3T3 mouse fibroblast cells imaging	[22, 43]
CdSe/ZnS core-shell	Detection of Her2 on breast cancer surface; Staining of cytoskeleton fibers in 3T3 mouse fibroblast cells; Nuclear antigen detection of human epithelial cells	[22]
CdSe/ZnS core-shell	DNA combing stained Sentinel Lymph Node in mouse tumor cells imaging	[37, 44]
CdSe/ZnS	F-actin filaments in fixed mouse fibroblasts imaging	[39]
Applications of QDs in neuroscience:		
CdSe	Lateral dynamics of QD-labeled glycine receptors	[45]
Amphiphilic p- sulfonated calixarene-coated CdSe/ZnS, CdTe	ACh detection	[9, 46]
CdSe/ZnS QDs	Imaging receptor mediated endocytosis in HeLa cells	[19]
CdSe/ZnS QDs	Imaging translocating proteins, cationic peptides, or specific membrane receptors	[39]
CdSe/ZnS QDs	Imaging glycine receptors, erbB/HER receptors	[39]
Poly(ethylene glycol)-coated CdSe/ Antibody functionalized QDs	Single cells of a Xenopus laevis embryo imaging	[39]
Tagged nerve growth factor (NGF) to QDs	Tracking the lateral diffusion of glycine receptors	[47]
Streptavidin-conjugated QDs	Labeling and tracking AMPA receptors on cultured hippocampal neurons	[47]

Until recently, cadmium-based QDs have been assuredly the most progressed ones, since the synthesis is straight-forward and their band gaps lie in the visible region of the spectrum, allowing for simple characterization [39, 40]. The inherent toxicity of cadmium has hindered its applicability, motivating research into alternative, less 'toxic' QD materials such as $CuInS_2$ [19]. Although various approaches have been reported for $CuInS_2$ synthesis including solvothermal synthesis, single-source precursor routes and hot injection techniques, which can produce high quality QDs [48, 49]; their biological applications have been faced with several problems. Since the synthesis is based on organic solvent; it produces hydrophobic $CuInS_2$ QDs that aggregate when exposed to the aqueous phase; not only causes the PLQY to be drastically diminished via a self-quenching mechanism, but also the solvent itself is toxic [50]. Moreover, the syntheses are very air sensitive and need many purification steps, which make them laborious, time-consuming and expensive. Many strategies are available to make biocompatible QDs including silanization, surface coating with water soluble ligands and encapsulation with block-copolymer micelles, phospholipid micelles, polymer beads, shells, or amphiphilic polysaccharides [22, 39] resulting in improper particles for neurotransmitter detection in the nanoscopic synaptic cleft owing to their size enlargement. As the best knowledge of authors, there are few methods for direct synthesis of biocompatible CIS QDs [51], while to tackle these problems, developing a proper synthesis method seems to be a necessity [50]. According to an extensive survey on the literature, a very efficient facile direct synthesis method producing biocompatible small size $CuInS_2$ QDs has been discovered in a work that Liu et al. [51] done in order to prepare water soluble high-quality ternary $CuInS_2$ QDs with mercaptopropionic acid (MPA) as the stabilizer by a novel hydrothermal synthesis route. It was used to label liver cancer cells. In another work, they used dopamine-functionalized $CuInS_2$ QD for urea detection in blood [20].

This article is concerned with the synthesis and characterization of CIS QDs as a less toxic alternative to the cadmium-based QDs that historically have dominated the literature; proposing their implementation in the neuroscience field specially neurotransmitters monitoring and detection due to the suitability and biocompatibility of this group of nanocrystals. So, in the first step we consider dopamine (one of monoamine neurotransmitters) to be tested. Then we will run experiments on the other monoamines such as norepinephrine (noradrenaline; NE, NA), epinephrine (adrenaline), histamine and serotonin (SER, 5-HT).

2. MATERIALS AND METHODS

2. 1. Materials and Apparatus All reagents were analytical grade and used directly without any purification. Copper (II) chloride dehydrate ($CuCl_2.2H_2O$), sodium hydroxide (NaOH), sulfourea ($CS(NH_2)_2$), mercaptopropionic acid (MPA), and indium (III) chloride tetrahydrate ($InCl_3.4H_2O$) were purchased from Sigma-Aldrich Corporation (St. Louis, MO, USA).

Transmission electron microscopy (TEM) experiments were performed on a Carl Zeiss AG (Oberkochen, Germany) - Zeiss EM900 TEM operating at 100 kV acceleration voltage. TEM samples were prepared by dropping the aqueous $CuInS_2$ solution onto carbon-coated copper grids and allowing the excess solvent to evaporate. FTIR spectra were recorded with a Beijing Rayleigh Analytical Instrument Corporation (BRAIC) (Beijing, China)- WQF-510 FTIR Spectrometer equipped with a DTGS detector (16 scans). UV-vis absorption spectra of CIS QDs were obtained using UV-VIS spectrophotometer, LAMBDA™ 25, Wavelength range 190-1100 nm, PerkinElmer Co. (Waltham, MA., USA). The photoluminescence spectra were measured by spectrofluorometer, Avaspec 2048 TEC, Avantes Co. (Apeldoorn, The Netherland).

2. 2. Synthesis of MPA-capped $CuInS_2$ QDs The synthesis of hydrophilic MPA-capped $CuInS_2$ QDs was achieved by adapting a recent literature hydrothermal synthesis method in which the surfactant MPA acts not only as both stabilizing ligand and source of sulfur for the nanoparticles, but also as the reaction solvent [20, 52]. The underlying principle behind this method is that excess of thiol promotes complete surface ligand coverage and therefore, good colloidal stability [19].

A wide range of indium and copper precursors has been shown to be compatible with this method. For the synthesis of CIS-based QDs in this work, indium (III) chloride and copper (II) chloride dehydrate were used, because of their demonstrated reactivity and solubility [19]. Due to this method, the reaction kinetics have all been optimized through control over various parameters such as the reaction duration, temperature, the concentration of precursors and the solvent composition. In a typical experiment, $CuCl_2.2H_2O$ (0.15 mmol) and $InCl_3.4H_2O$ (0.15 mmol) were dissolved in distilled water (10.5 ml) in a glass round-bottom flask (100 ml) then MPA (1.8 mmol) was injected into the solution, producing opaque yellow granules immediately (Figure 1, steps 1 and 2). The pH value of the mixture solution was adjusted to 11.3 by the drop-wise addition of 2 mol/L NaOH solution with gentle magnetic stirring.

During this process, the solution changed from turbid to clear pink (Figure 1, step 3). After stirring for 10 min, CS $(NH_2)_2$ (0.30 mmol) was dissolved in the solution. The Cu–to–In–to–S and Cu–to–MPA precursor ratios were 1:1:2 and 1:12, respectively [20, 52]. All the above mentioned experimental procedures were performed at room temperature, the flask was fitted with a condenser reflux column [19], then the solution was refluxed at 150 ℃ for 21 h after which cooled down to room temperature, quenching the reaction by a hydrocooling process. A purification method based on solvent extraction was used to separate unreacted precursors and reaction by-products from the as-synthesized hydrophilic QDs suspended in a nonorganic solvent [19]. Ethanol was added to the stock solution to obtain $CuInS_2$ QDs precipitate, and the process was repeated three times. The unreacted residues were removed by the cycled washing. The $CuInS_2$ QDs was dried at 60 ℃ for 4–6 h (Figure 1, step 4). The obtained powder was used for TEM and FTIR measurements [20, 52].

3. RESULTS AND DISCUSSION

3. 1. Structural Characterization The structural analyses of the as-synthesized $CuInS_2$ QDs were undertaken using TEM and FTIR.

TEM observations were employed to study the size of the ternary $CuInS_2$ QDs [52]. Figure 2A shows representative TEM micrograph of $CuInS_2$ QDs. The corresponding size distribution - obtained from TEM image - is also included in the Figure 2B while an inverse Gaussian function has been fitted to the distribution. By analysis of the TEM images, we determined the particle size of most of $CuInS_2$ QDs obtained from the fitting, which was approximately 2.3 nm.

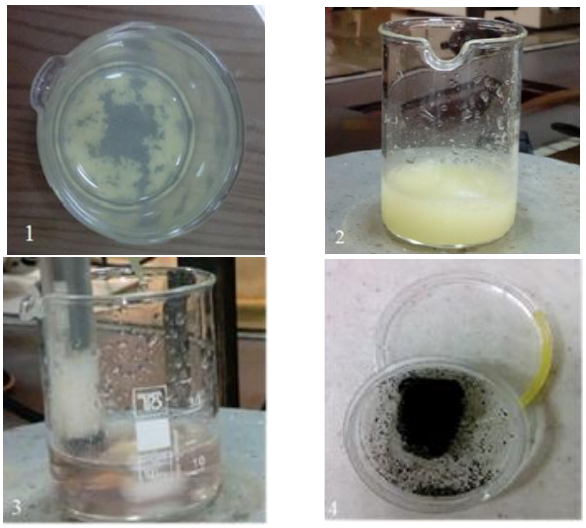

Figure 1. MPA-capped $CuInS_2$ synthesis steps

From the particle size distribution histogram (Figure 2B); it can be seen that the $CuInS_2$ QDs are nearly monodisperse with diameters ranging from 1.5 nm to 3.5 nm, and an average diameter of 2.28 nm.

As the heating step is very important in particle size, the common refluxed method in the heating step was compared with the autoclave method and its effect on the nanoparticle size. TEM observations indicated no significant difference in the $CuInS_2$ QDs size obtained from both heating methods [52], so the particles' synthesis could be done by both methods. As mentioned earlier, neurotransmitter release took place in the synaptic cleft with an approximately 20 ± 2.8 nm width [53]; TEM results confirmed the suitability of as-synthesized $CuInS_2$ QDs for the neuroscience applications specially neurotransmitter monitoring.

Because of their small dimensions, QDs have an inherently large surface to volume ratio, therefore, surface properties play a crucial role in their bioconjugation and also photoluminescence properties. As such, it is important to investigate the functionalization of the surface, determining the extent of surface coverage, the nature of the capping ligands, including their tendency to associate with surface atoms and surface defects. To further characterize the as-synthesized $CuInS_2$ QDs, FTIR has been carried out (Figure 3).

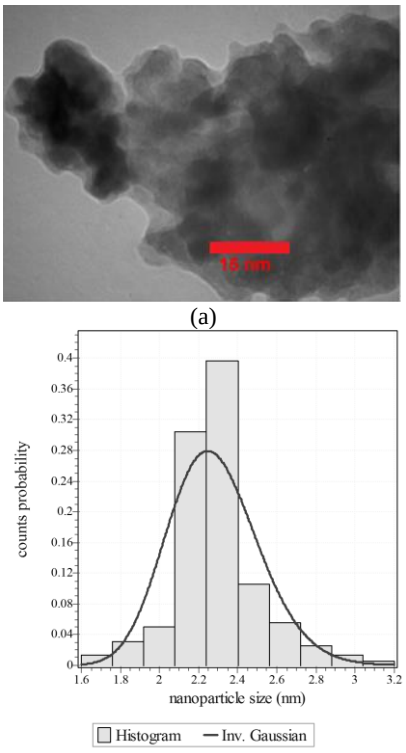

Figure 2. (a) TEM image of MPA-capped $CuInS_2$ QDs, (b) histogram of probability density function showing the size distribution of CIS QDs. The solid line represents an inverse Gaussian fit to the histogram

The FTIR spectra pointed that most functional groups of the as-synthesized QDs could be clearly found through the characteristic peaks of O–H (3436 cm^{-1} stretching vibration) and –COOH (2360 cm^{-1} asymmetric stretching vibration). The absence of the characteristic peak of S– H between 2550–2680 cm^{-1} indicated that the final $CuInS_2$ nanoparticles contain MPA on their surface, which might be caused by the covalent bonds between thiols and metal atoms [49, 52] of the ternary QDs.

3. 2. Optical Characterization The emissive properties of $CuInS_2$ QDs were explored with fluorescence spectroscopy; a typical PL spectrum for 2.3 nm QDs is shown in Figure 4.A. The narrow range of emission wavelengths was immediately obvious (600-750 nm) with a FWHM of ~49 nm. Importantly, this enables the QDs to emit within the biological window (650 nm – 1200 nm) [19], allowing for deeper penetration of the emitted light through biological tissue. The UV-vis absorption spectra of the as-prepared $CuInS_2$ QDs have been measured at room temperature. A typical absorption spectrum is also shown in Figure 4.B; showing absorption out at approximately 750 nm and tails off above 430 nm; a broad absorption band is observed together with an absorption tail at longer wavelengths. The absorption spectrum has no obvious absorption peaks like traditional binary QDs such as CdSe. The increasingly weakened absorption spectra below 430 nm indicated that unreacted material has been removed from the QD solution [48, 49, 54]. The application of these QDs for multiplexed biological imaging became possible owing to the combination of broad-band absorption and relatively narrow emission spectra. Furthermore, multiple QDs of different sizes (and therefore different PL spectral peak positions) can be excited with the same high energy (UV) source, yet emit at different wavelengths, facilitating separate components to be distinctly labelled [19].

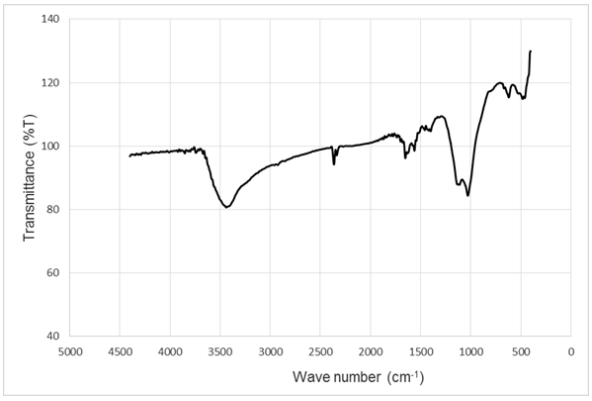

Figure 3. FTIR analysis of MPA-capped $CuInS_2$ QDs

Observations corroborate similar findings in the literature that the CIS QDs had a lower quantum yield compared to those reported for cadmium-based QDs [19]. This is attributed to the suppression of surface trap states, which arise from unsaturated bonds at the QD/solvent interface, and the ultra-fast non-radiative recombination associated with them, so determining the least amount of solvent needed to saturate the QDs' surface is very important. According to the aspect mentioned in the literature that the integrated area of the PL spectral peak, normalized to the absorption at the excitation wavelength, served as a measure of PL efficiency [19]; several experiments had been arranged. The molar excess of MPA in relation to Cu was varied between a factor of 6 and 16, whilst all other experimental conditions were kept constant. Figure 5 demonstrates that increasing molar excess of MPA would increase PL efficiency. The PL enhancement appears to reach a limit before a [Cu]/[MPA] value of approximately 1/10. So in this work, the optimal reactant molar ratio of [Cu]/[MPA] was chosen as 1/11, suggesting that this concentration is the minimum solvent required for complete surface coverage.

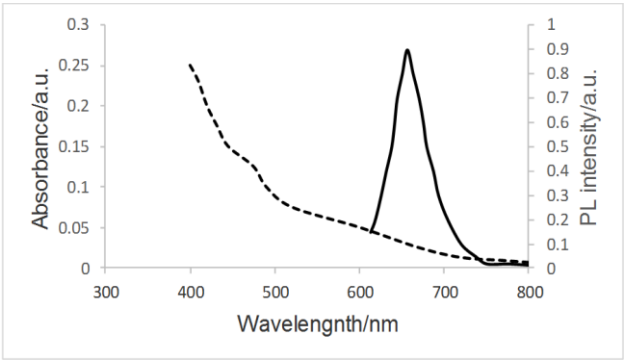

Figure 4. A) Fluorescence emission spectra (solid line) and B) UV-vis absorption spectra (dashed line) for as-synthesized $CuInS_2$ QDs

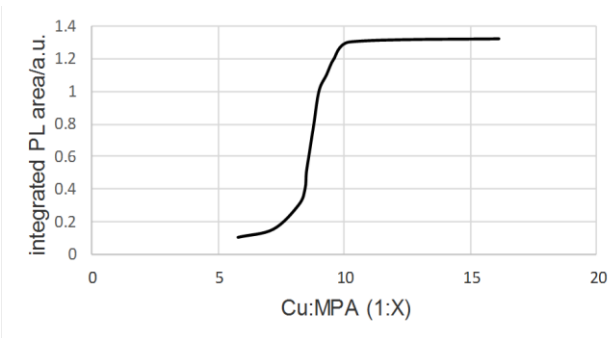

Figure 5. Plot of the relative integrated area of the PL spectral peak of MPA-capped CIS QDs with varying copper:MPA molar ratios

3. 3. Nanotechnology and Neuroscience: Two Converging Technologies Brain chemistry is by far the least known area of biochemistry research due to its complexity and difficulty to study, causing the brain research become the most expanding interdisciplinary research using the state of the art techniques to overcome limitations in order to conduct more accurate and effective experiments [55]. So it is imperative for any successful analysis method to have the following capabilities [19, 52, 53]:

High selectivity: Monitoring the chemical composition of the extracellular space, a rich chemical environment containing substances with extremely diverse chemical structure, *in vivo*, provides important information about brain function in health and disease; as such, the method ought to be able to distinguish analyte molecules in such a heterogeneous environment.

High sensitivity: The method should be able to detect target molecules having very low concentrations, in view of the fact that the concentrations of neurotransmitters exist both in intracellular and extracellular fluids needed to perform normal neurotransmitter functions are usually very low typically around μM or even down to nM.

Fast response: The dynamic signal transduction process for neurotransmitters could be initiated and completed in a few milliseconds. Under this time scale, any method that cannot respond fast enough would not be able to reveal the true behavior of neurotransmitters.

Miniaturization: As the distance between the pre- and postsynaptic cells is at the nanometer range, in order to obtain representative data of neurotransmitters at good spatial resolution for such extremely tiny space, the detecting ability of the method should be able to match such dimensions.

CIS QDs: a novel tool for neurotransmitter monitoring

With good sensitivity, selectivity, temporal and spatial resolution; taking advantage of the intrinsically low toxic CIS QDs have been proposed in this article for neurotransmitters monitoring. Also applying a novel facile hydrothermal route for their synthesis is a trump card. In order to support the proposal, several reasons have been discussed in the following:

$CuInS_2$ QDs have emerged as particularly exciting materials for the synthesis of a new class of fluorescent probes, not only since the inherent toxicity of the readily available constituent elements, copper and indium, appears to be significantly lower than that of cadmium and lead, but also due to the unique structural and electronic properties that arise from the composition and structure of ternary semiconductor compounds in general [19, 21]. On the other hand, the previous common methods for QDs synthesis are based on organic solvents following reactions performed at high temperatures [19, 39], producing hyrophobe nanoparticles which aggregate in biological media, causing drastic reduction of the PLQY owing to QDs self-quenching [56]. In addition, organic solvents used as stabilizing agents can be unfavorable for sensing purposes, since these coatings can act as a barrier for the diffusion of the analyte to the surface of the nanoparticle [9]. Direct hydrothermal synthesis of CIS QDs offers advantages such as lower reaction temperature with comparable PLQY, does not use toxic and expensive organometallic reagents, does not need any surface functionalization during synthesis without further treatment resulting in no longer producing harmful bi-products, comparatively smaller particle size and tunable nanoparticle size and morphology by controlling the precursors' concentration, temperature and time of reaction [19, 40].

CIS QDs represent a new tool of significant potential in neuroscience research. Because of their extremely small size and optical resolution, they are well suited for tracking the molecular dynamics of intracellular and/or intercellular molecular processes over long time scales. For example, they are useful for experiments that are limited by the restricted anatomy of neuronal and glial interactions, such as the small size of the synaptic cleft. These properties are difficult to achieve using other techniques or approaches so they can be applied to visualize, measure, and track individual molecular events using fluorescence microscopy.

4. CONCLUSION

This article is concerned with the synthesis and characterization of CIS QDs as a less toxic alternative to the cadmium-based QDs that historically have dominated the literature, proposing their implementation in the neuroscience field specially neurotransmitters monitoring and detection due to the suitability and biocompatibility of this group of nanocrystals. A well-established synthesis method in the literature was shown to be easily modified to produce these QDs with the desired surface chemistry. The structural and optical properties of CIS QDs is characterized. TEM measurements showed the average nanocrystal size was 2.28 nm. FTIR results have indicated that the surface of the synthesized nanoparticles is functionalized with MPA capping ligands. Spectrophotometery demonstrated that CuInS2 QDs are a widely useful optical material for molecular imaging due to their large absorption and bright emission spectra.

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Nanotechnology and Neuroscience Convergence: A Novel Tool for Neurotransmitters Monitoring

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P A P E R I N F O

Paper history:
Received 02 November 2016
Received in revised form 09 January 2017
Accepted 09 February 2017

Keywords:
Neurotransmitter
Synaptic Transmission
Bioconjugating
Bioimaging
$CuInS_2$ Quantum Dots
Photo-luminescence

چکیده

از آنجا که انتقال‌دهنده‌های عصبی به‌طور قابل توجهی فعالیت مغز را تحت تاثیر قرارمی‌دهند، درک ما از مغز انسان تا زمانی که همه جنبه‌های مربوط به آن‌ها روشن شود، ناقص باقی خواهد ماند. یکی از چالش‌های اصلی در تحقیقات علوم اعصاب و درمان آشکار شدن سازوکار رهایش انتقال‌دهنده‌های عصبی و تنظیم مقدار و زمان رهایش آن‌ها می‌باشد. علی رغم مطالعات بسیار زیادی که در این زمینه صورت گرفته است تا کنون روش کارآمدی برای ردیابی و مشاهده این مواد شیمیایی–عصبی با اندازه بسیار کوچک وجود ندارد. پیشرفت‌های اخیر در علم نانومواد با اتصال نقاط کوانتومی به مولکول های زیستی سبب پیدایش گروه جدیدی از نشانگرهای فلورسنت شده است. نقاط کوانتومی بر پایه کادمیم در تصویرسازی زیستی بیشترین پیشرفت را داشته‌اند اما به دلیل سمیت بالا، آینده آن‌ها در هاله‌ای از ابهام قرار دارد لذا توجه محققان به ترکیبات غیر سمی سه تایی $CuInS_2$ جلب شده است. در این مقاله کاربرد جدیدی از نانوذرات $CuInS_2$ در علوم اعصاب پیشنهاد گردیده است. بر این اساس از روش سنتزی که به تازگی توسعه یافته با به‌کارگیری مرحله رفلاکس استفاده شد. تجزیه و تحلیل ساختاری و سطحی TEM و FTIR نشان داد که اندازه نانوبلورهای به‌دست آمده در محدوده ۱/۶–۳/۲ نانومتر قرار دارند و سطح آن‌ها به خوبی با لیگاند مرکاپتو پروپیونیک اسید عامل‌دار شده است. آنالیز طیف سنجی نانوذرات، خواص نوری مطلوبی شامل طیف جذب گسترده و طیف نشر باریک به ترتیب ۲۵۰ و ۱۵۰ نانومتر و پیک فتولومینسانس ۶۵۶ نانومتر و FWHM ۴۹ نانومتر را نشان داد. همه این موارد تایید می‌کنند که نقاط کوانتومی برای ردیابی انتقال‌دهنده‌عصبی درفضای کوچک شکاف سیناپسی بسیار مناسب است. همچنین پیشنهاد شد که حداقل غلظت مس نسبت به لیگاند مورد نیاز برای پوشش کامل سطح به ترتیب ۱ به ۱۱ می‌باشد.

***doi**: 10.5829/idosi.ije.2017.30.02b.01*