Antidepressant drug-protein interactions studied by spectroscopic methods based on fluorescent carbon quantum dots

Reshma a, Sandeep K. Vaishanav a,b, Toshikee Yadav a, Srishti Sinha a, Swapnil Tiwari a, Manmohan L. Satnami a, Kallol K. Ghosh a,*

a School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur, C.G., 492010, India
b State Forensic Science Laboratory, Raipur, C.G., 492013, India

ARTICLE INFO

Keywords:
Physical chemistry
Materials chemistry

ABSTRACT

A highly sensitive fluorescent carbon quantum dots (CDs) was designed to measure the interaction of antidepressant drugs and serum albumins (SA). In present investigation the interaction of bovine serum albumin (BSA) and human serum albumin (HSA) with antidepressant drugs viz. amitryptiline hydrochloride (AMT), chlorpromazine hydrochloride (CPZ) and desipramine hydrochloride (DSP) bioconjugated on CDs have been studied by different spectroscopic techniques i.e., Fluorescence, UV-Visible, Dynamic light scattering (DLS) and FT-IR. The CDs were prepared by one-pot method using glucose and PEG-200. The developed CDs showed blue luminescence under irradiation with ultra-violet. The Stern-Volmer quenching constant (Ksv) indicates the presence of static quenching mechanism. The apparent binding constant (K_a) between antidepressant drugs with complex of SA-CDs have been determined. These results illustrated that CPZ shows strong binding with HSA. As further analyzed by FT-IR spectroscopy and DLS technique, the results suggested induced conformational changes on SA, thus confirming the experimental and theoretical results. Thus, a thorough knowledge of the energetics of drug-protein affinities in presence of CDs as attempted in this work is vital in giving way for appropriate drug delivery.

1. Introduction

Fluorescent carbon nanodots have received increasing attention in a wide variety of analytical and biomedical applications owing to their outstanding properties such as minimal toxicity, superior biocompatibility, tunable photoluminescence and good water solubility [1, 2, 3, 4]. The binding mechanism of proteins with ligands from last few years have shed light on different areas of research and its important applications in numerous fields of science, such as the development of new biomaterials, biochemistry, food chemistry or pharmaceutical sciences [5, 6, 7, 8, 9, 10]. The nature of interaction between the drug molecule and protein gives new opportunity for the development of new drugs. Since drugs are the compounds which are carried by albumin, it is necessary to study the interaction of new drug with protein [11, 12, 13, 14, 15]. Serum albumins are a model globular protein which play a key role for acting as a carrier for several endogenous compounds. It has proved the most valuable invented globular proteins, used for transportation and metabolism of many biologically active compounds in the body [16, 17, 18]. Serum albumin has a well-established structure, having physicochemical properties, a versatile binding capacity stability and water solubility [19, 20]. In the present scenario bovine serum albumin (BSA) has created an extensive area of research because of its presence in blood plasma of animals. It consist a single polypeptide chain of 583 amino acids and contains 17 cysteine residues (eight disulide bonds and one free thiol). It is divided into three specific binding sites (I, II and III) for high-affinity of drugs. Every sites is consists of two subdomains (A and B). Human serum albumin (HSA) contributes about 80% of the osmotic pressure of blood [21, 22]. It bears residue of 585 amino acids with molar mass of 66,411 g mol⁻¹ having 17 disulfide bridges and free thiol (SH) group. Moreover, HSA consist of single tryptophan (TRP 214) present in subdomain IIA [23, 24, 25]. The theme has a better insight for research fields such as clinical medicine, chemistry and life sciences.

A tricyclic antidepressant drug (TCA) category of drug amitryptiline hydrochloride (N,N-dimethyl-3-(2-tricyclo[9.4.0.03,8]pentadeca-1(15),3,5,7,11,13-hexaenylidene)propan-1-amine; hydrochloride), desipramine hydrochloride (3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N-methylpropan-1-amine; hydrochloride) achlorpromazine hydrochloride (3-(2-chlorophenothiazin-10-yl)-N,N-dimethylpropan-1-amine;...
hydrochloride) has been widely used to treat major depression sickness, manic disorder and also for schizophrenia [26, 27, 28, 29]. The outcomes of the study of interaction of drug with SA and plasma of human or living tissue for diagnosing disease, controlling the amount of drug, obtaining optimum therapeutic concentration, controlling its side effects, evaluating the stability as well as the toxicology of the drug and complications of drug abuse.

Shahabadi et al. [29] observed the interaction of venlafaxin hydrochloride with bovine serum albumin (VEN-BSA) and revealed that the Stern-Volmer quenching constant \(K_{sv}\) is inversely correlated together with temperature and concentration. This suggests the probable quenching mechanism of binding reaction which is initiated due to complex formation. Field et al. [30] studied a development of quantum dots (QD) based-protein bioconjugate that provides for extracellular control of multicomponent drug release system. These results confirmed by time-resolved measurements of the QD donor excited state lifetime before and after maltose-induced conjugate release. Chamani and his co-workers [31] reported the binding of ciprofloxacin to human serum albumin (HSA) in the presence and absence of silver nanoparticles of three sizes as well as their various behaviors in drug delivery. These consists of, for example, the use of incident excitation light for the photocleavage of labile linkers and the application of magnetic, ultrasonic, or radiofrequency fields to facilitate drug release from properly sensitive nanocarriers. However, these drug release modalities are not without their margins [32, 33, 34]. The current researchers established that control intracellular release of drug cargos from nanobioconjugate carrier is critical for the successful implementation of nanoparticle (NP)-mediated drug delivery (NMDD) [35, 36].

In biophysical research, the most important idea is the interaction of drug molecule with biological molecule. Studies on drug-protein interaction are important in pharmacology and pharmacokinetics. Generally, the binding nature of drug-albumins is dynamic and reversible [37, 38, 39, 40]. We have already reported in previous paper [41, 42, 43] the interaction of serum albumins with fluorescent carbon quantum dots, surfactants and antidepressant drugs by surface tensiometer, conductivity meter and spectroscopic techniques. Herein, the present investigation focused on the interaction of serum albumins (Scheme 1) with antidepressant drugs (Scheme 2) in absence and presence of carbon quantum dots (CDs). The carbon quantum dots (CDs) synthesized by one-pot method using PEG (Polyethylene glycol-200) and glucose. The analysis of binding of different ligands with protein using multispectroscopic techniques such as fluorescence measurement, UV-Vis absorption, dynamic light scattering (DLS) and Fourier transform infrared spectroscopy (FT-IR), which have high sensitivity, reproducibility, cost effective and convenience. It plays emphasis role on the special binding site and the effect of antidepressant drugs on the secondary structure of serum albumins.

### 2. Experimental

#### 2.1. Materials

Human serum albumin (HSA) and bovine serum albumin (BSA) (purity 99.96%) and antidepressant drugs amitryptiline hydrochloride (AMT), desipramine hydrochloride (DSP) and chlorpromazine hydrochloride (CPZ) (purity 99.88%) were procured from Sigma Aldrich Pvt. Ltd. Bangalore. Glucose and polyethylene glycol-200 (PEG-200) procured from Sigma Aldrich Pvt. Ltd. Bangalore. All chemicals were employed as purchased and their standard solutions were prepared using Millipore water. All serum albumin solutions were prepared by phosphate buffer solution.

#### 2.2. Methods

##### 2.2.1. Synthesis of carbon quantum dots (CDs)

The CDs was synthesized by one-pot method [41]. In a beaker 1.0 g glucose and 15 ml PEG-200 was added, and dissolve it in 30 ml Milliopore water followed by stirring for 10 minutes, till a clear solution was obtained. Now the solution was heated in a hot air oven for 1 hr at 160 °C. A pale yellow color solution was obtained. This solution was kept for dialysis by dialysis membrane 500 cutoffs for one day and again dialysis by dialysis membrane 1000 cutoffs. The resulted CDs stored at 4 °C.

##### 2.2.2. Fluorescence

The fluorescence quenching mechanisms were investigated on a Cary Eclipse Fluorescence Spectrophotometer using a quartz cell with 1.0 cm path length in a thermostatically controlled cell holder at 300K. The excitation wavelength kept for BSA and HSA fluorescence was 280 nm and its emission spectra were scanned in the range of 290–450 nm. Both excitation and emission slit widths were fixed at 5 nm. The fluorescence quenching measurements have been also performed for determining the binding constant (\(K_d\)) and Stern-Volmer constant (\(K_{sv}\)).

##### 2.2.3. UV-visible spectroscopic measurement

The absorption measurements of solutions were carried out by Carry-50 UV-Vis spectrophotometer using a matched pair of quartz cell (path length: 1 cm) at 27 °C. The absorption spectra were scanned in the range of 240–450 nm. The absorbance measurements were performed keeping the concentration of serum albumins and varying the concentration of drugs from 0 to 0.55 mM and different concentration of CDs.

##### 2.2.4. FT-IR spectroscopy

Using diffuse reflectance method FT-IR spectra were taken on a Nicolet iS10 Fourier transform infrared spectroscopy (Thermofisher) by KBr pellets as a background. The FT-IR spectra of HSA and BSA in the

---

**Scheme 1.** Structure of serum albumins (Source – [http://www.rcsb.org/](http://www.rcsb.org/)).
presence and absence of drug at 27 °C were recorded in the range of 1500–1700 cm⁻¹.

2.2.5. Dynamic light scattering (DLS)

The average hydrodynamic diameter and zeta potential of the formulated quantum dots were determined by Dynamic Light Scattering (DLS) analysis using ZetaSizer Nano ZS90 (Malvern Instruments Limited, Japan) equipped with a 4.0 mW He-Ne laser operating at 630 nm. For the particle size measurements 1 ml sample of quantum dots dispersion were taken in disposable cuvettes. All measurements were carried out after dispersing the quantum dots in appropriate volume of water at 300 K, at detection angle 120 °C for zeta potential.

3. Results and discussion

3.1. Characterization of CDs

The TEM images of the prepared CDs was measured by JEOL, JEM-2100 F operated at accelerating voltage 200 kV. Monodispersed spherical shape CDs have been observed (Fig. 1a). FT-IR spectroscopy was used to determine the functional groups on the surface of the found CDs. As shown in Fig. 1c, the strong and broad absorption band 3397 cm⁻¹ ascribed to the stretching vibrations of the O–H/N–H. UV-Vis absorption spectrum of the synthesized CDs comprising an absorption peak at 340 nm corresponding to the π-π* transition of the aromatic sp² domain. The CDs exhibited an obvious, narrow and symmetrical emission spectrum with a strong emission, maximum at 437 nm shown in Fig. 1b.

3.2. Binding constant and binding capacity

3.2.1. In absence of CDs

Fluorescence spectroscopy has been mostly used in the investigation of molecular interactions between ligands and proteins. The variety of parameters related to binding mechanism of antidepressant drugs with serum albumins have been investigated by means of fluorescence measurements. Serum albumins have three intrinsic fluorophores residues tryptophan (Trp), tyrosine (Tyr) and phenylalanine (Phen) [43]. Generally, the Trp alone contribute to intrinsic fluorescence, because Phen has a very low quantum yield and the fluorescence of Tyr get completely quenched when ionized. Therefore, the fluorescence of BSA and HSA regularly decreases with increasing concentration of drugs but does not show any significant shift of the emission at maximum wavelength. The fluorescence spectra of BSA and HSA with varying concentration of antidepressant drugs are shown in Fig. 2 (a and b).

In static quenching, when drug molecules bind independently to a set of equivalent sites on a protein, the relation between fluorescence quenching intensity of serum albumins and concentration of drugs can be calculated using following Eq. (1).

$$\log \left( \frac{F_0 - F}{F} \right) = \log K_a + \alpha \log [Q]$$

(1)

On plotting graph, log(F₀ − F)/F versus log [Q], the number of binding sites (n) and binding constant K_a have been obtained Fig. 2 (d). In Table 1, different values of binding constant K_a and binding sites have been listed for drug associated with serum albumins. The obtained data
The proximity of the SA tryptophan residues [44, 45]. The received values of the combined binding constant equation can be registered as well in case of large molecules, such as proteins. Hence, to study the interaction of new drug with protein, it becomes necessary to study the interaction of new drug with protein.

Moreover, in the event of proteins the positive deviations from the fluorescence quenching, or the existence of just a single binding site in serum albumins for drugs. Hence, drugs most likely bind to the hydrophobic pocket spotted in subdomain IIA. The value of correlation coefficient ($R^2 = 0.999$) shows the interaction of drugs with serum albumins the site binding model underlying Eq. (1).

From Table 1, it is evident that serum albumins were bound strongly with CPZ as compared to AMT and DSP, due to the presence of phenothiazine ring. The fluorophore commonly excited from the ground state ($S_0$) to the first singlet state ($S_1$) due to more $\pi$ character, which the electron density exchanged from sulfur atom of the center ring of phenothiazine to the benzene rings [39, 40]. Since drugs have been carried by albumin it becomes necessary to study the interaction of new drug with protein.

Moreover, in the event of proteins the positive deviations from the fluorescence quenching extent or domination of fluorescence process by one single residue (distance-dependent quenching due to a single molecular interaction) [31]. Fig 2 (a and b) depicts the fluorescence spectra of BSA and HSA fluorescence quenched by the drug. The plot of SA-drug systems shows an upward curvature, not only at higher drug concentrations, what could indicate or the combined fluorescence quenching, or the existence of more than one binding site with different accessibilities for drug in the proximity of the SA tryptophan residues [44, 45]. The received values of Stern-Volmer $K_{SV}$ are distinct compared with the values of binding constant $K_a$ for the system studied. Such results could be the consequence of concurrent formation of a coordinate bond between groups on the protein surface.

### 3.2.2. In presence of CDs

In the presence of CDs, there are two types binding sites with various affinities that depend on the size of quantum dots. It is revealed that the interaction between SA and drugs in the presence of carbon dots have different behaviors; therefore CDs have various applications in protein solution that can be related to their different hydration layers. $K_a$ is a measure of the binding of the proteins to the drugs, suggesting that the $K_a$ value for SA-drug increasing in the presence of CDs at $\lambda_{ex} = 278$ nm. These results led to the conclusion that the interaction between drug and SA changed after addition of CDs to the SA-drug complex. Consequently, the CDs caused a stronger complex to be established. The interaction behavior of SA-drug changed with the presence of CDs in the ternary systems at $\lambda_{ex} = 280$ nm was higher than at $\lambda_{ex} = 295$ nm, because at $\lambda_{ex} = 280$ nm both Tyr and Trp were excited, whereas at $\lambda_{ex} = 295$ nm only Trp was excited. The values of $K_a$ and $n$ are listed in Tables 1 and 2. As can be seen, the interaction between SA and drug in the absence and presence of CDs respectively. However, to the best of our knowledge, so many works reported in related to drug-protein interaction, but drug–protein interaction in presence of nanoparticles a least research articles published.

### 3.3. Fluorescence quenching mechanism

#### 3.3.1. In absence of CDs

The fluorescence quenching basically divided into dynamic quenching and static quenching. Dynamic quenching represents from collision

#### Table 1

| S.No. | System       | $K_w \times 10^{-5}$ | $K_a \times 10^{-5}$ | N   | R²   |
|-------|--------------|----------------------|----------------------|-----|------|
| 1.    | HSA + AMT    | 10.02                | 10.9                 | 1.089 | 0.990 |
| 2.    | HSA + DSP    | 5.08                 | 6.31                 | 1.193 | 0.992 |
| 3.    | HSA + CPZ    | 13.38                | 13.5                 | 1.351 | 0.996 |
| 4.    | BSA + AMT    | 5.93                 | 5.98                 | 0.536 | 0.995 |
| 5.    | BSA + DSP    | 1.37                 | 1.44                 | 0.724 | 0.989 |
| 6.    | BSA + CPZ    | 25.6                 | 31.9                 | 1.114 | 0.997 |

#### Table 2

| S.No. | System       | $K_w \times 10^{-5}$ | $K_a \times 10^{-5}$ | N   | R²   |
|-------|--------------|----------------------|----------------------|-----|------|
| 1.    | HSA + AMT + CDs | 12.07               | 11.1                 | 1.032 | 0.993 |
| 2.    | HSA + DSP + CDs | 5.69                | 7.22                 | 1.251 | 0.996 |
| 3.    | HSA + CPZ + CDs | 15.03               | 15.2                 | 1.353 | 0.998 |
| 4.    | BSA + AMT + CDs | 5.00                | 5.54                 | 0.810 | 0.982 |
| 5.    | BSA + DSP + CDs | 2.78                | 2.36                 | 0.824 | 0.979 |
| 6.    | BSA + CPZ + CDs | 29.1                | 35.3                 | 1.222 | 0.998 |
encounters between fluorophore and quencher, whereas quenching by formation of a complex between quencher and fluorophore predating excitation shows the static quenching. The quenching mechanism of serum albumins with drugs is static in nature. It shows the fluorescence intensity of BSA and HSA remains constant with increasing drug concentration because drug can bind to the HSA and BSA [42, 43, 44]. The quenching process of BSA and HSA with drugs have been studied and determined by the following equation [45].

\[
\frac{F_0}{F} = 1 + K_{SV}[Q]
\]

(2)

Where \(F_0\) and \(F\) are the fluorescence intensities in the presence and absence of quencher, respectively. \(K_{SV}\) is the Stern-Volmer quenching constant obtained from linear Stern-Volmer plot of \(F_0 / F\) against \([Q]\) (equation.2) at 300 K temperature. The Stern-Volmer plots of the quenching of HSA and BSA tryptophan residue by drug have been represented Fig. 2 (c). \(K_{SV}\) is the Stern-Volmer static quenching constant, based on the experimental data. AMT, DSP and CPZ, the quenching constant \(K_{SV}\) were obtained and listed in Table 1.

3.3.2. In presence of CDs

Serum albumins have the capability to restore the CDs intensity by

Fig. 3. Fluorescence spectra represent the (a) CDs-CPZ and (b) CDs- AMT system in the presence of different serum albumins; (c) Stern-Volmer plots of fluorescence quenching of HSA by drugs (\(\lambda_{max} = 280\) nm) (d) Plots of log\((F_0 - F) / F\) vs. log \([Q]\) for binding constant of HSA \(\lambda_{max} = 280\) nm at room temperature (pH 7.6).

Fig. 4. Absorption spectra of (a) BSA and (b) HSA in the presence of various concentration of drug (\(\lambda_{max} = 280\) nm) at 300 K. (c) Benesi-Hildebrand plot using changes in absorption spectra of HSA and (d) BSA [measured at 280 nm for AMT, CPZ and DSP] at room temperature (pH 7.6).
interaction with the quencher absorbed on CDs surfaces. As shown in Fig. 3a and 3b drug quenched the serum albumins fluorescence intensity then increased almost proportionally with the increase of CDs concentration added in the SA-Drug system. Studies of binding site with warfarin and ibuprofen by fluorescence spectroscopy reported in our previous article [41].

The HSA/BSA concentration-dependent fluorescence intensity can therefore be utilized to develop the CDs fluorescence intensity based method for the determination of equilibrium parameters for HSA/BSA-Drug interaction. The binding constant (K) of drug molecule binding with HSA/BSA can be determined simultaneously shown in Fig. 3d. According to previous paper [46, 47, 48], we assume that a drug molecule bind with a binding site on the serum albumins to form a complex. The linear regression of a plot of F0/F against [Q] shown in Fig. 3c. The results obtained by all method were comparable with the previous by spectrophotometric methods [48, 49]. Table 2 shows the binding constant (Kx), Stern-Volmer quenching constant (Ksv) and binding capacity (n) and correlation coefficient (R2) of SA-drug-CDs systems at temperature 300 K.

3.4. UV-visible studies

UV-Vis spectra of HSA-Drug and BSA-Drug systems have been recorded to investigated complex formation between protein and drug molecules and to explore the structural changes. UV absorption spectra of HSA and BSA proteins in the absence and presence of drugs have been shown in Fig. 4 (a and b). The absorbance of HSA-Drug and BSA-Drug system decreases with increasing concentration of drug, furthermore, the spectra found to be deshifted from 300nm to 350 nm at the maximum absorption wavelength of protein. The absorption peak shows around 278 nm which caused by the transition π-π* of aromatic residues in BSA and HSA are raised. The absorption maxima corresponding to drug-protein complex instead maximum peak position of a complex between protein and drug and the change in polarity around one tryptophan residue [20, 47].

The binding constant of the drug-protein complex were also determined using UV-vis spectroscopic method by the equation given below [47].

\[
\frac{1}{A - A_0} = \frac{1}{K(A_{\text{max}} - A_0)[Q]} + \frac{1}{A_{\text{max}} - A_0}
\]

where, A0, A,  

Table 3 Binding constant (K) and correlation coefficient (R²) of BSA and HSA with antidepressant drugs at 300 K (pH 7.6).

| S. No. | System | K x 10⁻⁹ M | R²      |
|-------|--------|-----------|---------|
| 1.    | AMT    | 3.24      | 0.982   |
|       | BSA    | 0.64      | 0.980   |
| 2.    | CPZ    | 6.84      | 0.996   |
|       | BSA    | 1.08      | 0.991   |
| 3.    | DSP    | 3.60      | 0.994   |
|       | BSA    | 0.80      | 0.998   |

3.5. FTIR spectra

The Drug-Protein interaction and conformational changes can be interpreted from FTIR spectra as depicted in Fig. 5. Infrared spectra were taken employing diffuse reflectance accessory with Deuterium triglycine sulphate (DTGS) detector at resolution of 4 cm⁻¹. The infrared spectrum of pure BSA and HSA and their interaction with one of the drug, AMT has been shown in Fig. 5. The protein structures have been studied and interpreted through the various amide groups in peptide group, however,
of all the amide modes the amide I is most widely studied. The I and II peak of amide have been occurred at the range of 1500–1600 cm\(^{-1}\) and 1600-1700 cm\(^{-1}\) respectively. For the significant study of secondary structure of proteins enlighten more usefulness of amide band I. Hence amide bond is more sensitive to the changes in the secondary structure of protein [50, 51].

Due to the stretching of the C=O bonds, the protein amide I bond is observed at 1655 cm\(^{-1}\) and the amide II bond, due to the coupled interaction of C-N stretching and N-H bending is observed at 1549 cm\(^{-1}\). It is evident from the figure that the proteins amide I band appeared at FTIR spectrum of free HSA and BSA in phosphate buffer solution and the difference absorption spectra upon binding with antidepressant drug are given in Fig. 5 for (A) BSA and for (B) HSA respectively. It shows that the peak position of amide I was shifted from 1670 to 1643.1 cm\(^{-1}\) in HSA-Drug system, while that of amide II was shifted from 1554.4 to 1567.8 cm\(^{-1}\) in HSA-Drug systems. These data shows the antidepressants drug has interacted with both serum albumins and the secondary structural changes leading to conformational changes.

3.6. The stoichiometry of serum albumins attached carbon quantum dots

Dynamic light scattering (DLS) experiment was conducted with particles dispersed and size distribution during the assembly of CDs-SA-Drug. The variation in size, scattering intensities observed for antidepressant drugs and CDs. Particle size distribution was found in the range of 1–1000 nm. The results from DLS measurements showed that the size (diameter) of the nanohybrids did not change with the increasing number of serum albumins per CDs and antidepressant drugs, upon addition of various molar ratio of SA-antidepressant drugs. DLS determinations showed that the negative surface charge of the quantum dots neutralized upon adsorption of the serum albumin and drug. Generally, the \(\zeta\) potential of CDs was reduced when SA-drug were bond that the surface, further increase of the drug concentration did not lead to significant changes in the DLS as shown in Fig. 6. Moreover, the data revealed that the nanohybrid is a complex between CDs and protein which were formed due to electrostatic interactions of the negatively charged CDs and the cationic “hot spot” around the active site of SA antidepressant drugs. It also revealed the exact amount of SA-antidepressant drugs adsorbed over each CDs.

4. Conclusion

In the present work, the binding of antidepressant drugs (AMT, CPZ, DSP) to serum albumins (BSA/HSA) were carried out by employing spectroscopic techniques under physiological conditions. The intrinsic tryptophan fluorescence of serum albumins turns out with a chance to be a vital tool for better understanding. The results enlighten the primary information on the binding of drugs to serum albumin protein. The experimental data showed that the Stern-Volmer quenching constant \(K_{sv}\) is inversely correlated; static quenching was confirmed to result in the fluorescence quenching. The results of UV-Visible spectra indicate that the conformational changes of BSA/HSA molecules are change significantly in the presence of antidepressant drugs. None of this method for enhancing fluorescence intensity of CDs by modifying CDs with serum albumins by virtue of the activated effect of antidepressant drugs was proposed. In this study firstly biconjugated quantum dots with serum albumins further studies the interaction of bioconjugated SA with antidepressant drugs. The drug-protein interaction based on quantum dots of biological significance is evident since albumin serves as a carrier of protein carrier for multiple drugs.

Declarations

Author contribution statement

Reshma Sahu: Performed the experiments; Analyzed and interpreted
the data; Wrote the paper.
Sandeep K Vaishnav, Toshikazu Yadav, Srishti Sinha: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.
Swapnil Tiwari: Performed the experiments; Analyzed and interpreted the data.
Mannomon Satnami, Kallool G. Ghosh: Conceived and designed the experiments.

Funding statement
This work was supported by DST-FIST [no.SR/FST/CSI-259/2014(C)] and CCOST, Raipur (Chhattisgarh) [no.2744/CCOST/MRP/2015] and UGC New Delhi [no.43–183/2014 (SR)].

Competing interest statement
The authors declare no conflict of interest.

Additional information
No additional information is available for this paper.

Acknowledgements
Authors are grateful to Prof. M. K. Deb, Head, School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur (C.G.) for providing laboratory facility.

References
[1] S.Y. Lim, W. Shen, Z.Q. Gao, Carbon quantum dots and their applications, Chem. Soc. Rev. 44 (2015) 362–381.
[2] A.D. Zhao, Z.W. Chen, C.Q. Zhao, N. Gao, J.S. Ren, X.G. Yang, Recent advances in bioapplications of C-dots, Carbon 85 (2015) 309–327.
[3] R.M. Freire, N.D.B. Le, Z. Jiang, C. SooKim, V.M. Rotello, P.B.A. Fechine, Carbon quantum dot-based nanoprobes for metal ion detection, Sensor. Actuator. B 255 (2018) 2729–2732.
[4] A.O. Elzoghby, W.M. Samey, N.A. Elgindy, Protein-based nanocarriers as promising drug and gene delivery systems, J. Control. Release 161 (2012) 38–49.
[5] S.N. Baker, G.A. Baker, Luminescent carbon nanodots: emergent nanolights, Angew. Chem. Int. Ed. 49 (2010) 6726–6744.
[6] Y. Huang, F. Yu, Y.S. Park, J. Wang, M.C. Shin, H.S. Chung, V.C. Yang, Co-administration of protein drugs with gold nanoparticles to enable percutaneous delivery, Biomaterials 31 (2010) 9085–9094.
[7] B. Wu, R. Zhu, M. Wang, P. Liang, Q. Tian, S. Wang, Fluorescent carbon dots from antinflammatory drug etoposide for bioimaging in vitro and in vivo, J. Mater. Chem. B 5 (2017) 7796–7800. http://pubs.rsc.org/en/results?searchtext=
[8] F.H. Cincotto, D.L.C. Golinnelia, S.A.S. Machadhob, F.C. Moraes, Electrochemical sensor based on reduced graphene oxide modified with palladium nanoparticles for determination of desipramine in urine samples, Sens. Actuators. B 239 (2017) 488–493.
[9] L.D. Field, S.A. Walper, K. Susumu, G. Lasarte-Aragonés, E. Oh, L.D. Medintz, J.B. Delehanth, A quantum dot-protein bioconjugate that provides for extracellular control of intracellular drug release, Bioconjug. Chem. 29 (2018) 2455–2467.
[10] A.A. Bhatchattarya, T. Grune, S. Curry, Analysis reveals common modes of binding of medium and long-chain fatty acids to human serum albumin, J. Mol. Biol. 303 (2000) 721–732.
[11] I. Pétips, T. Grune, A.A. Bhatchattarya, S. Curry, Crystal structures of human serum albumin complexed with monounsaturated and polyunsaturated fatty acids, J. Mol. Biol. 314 (2001) 955–960.
[12] J. Ghuman, P.A. Zunszain, I. Pétips, A.A. Bhatchattarya, M. Otogari, S. Curry, Structural basis of the drug-binding specificity of human serum albumin, J. Mol. Biol. 353 (2005) 38–52.
[13] R. Beauchemin, C.N.N. Soukop-Koukis, T.J. Thomas, T. Thomas, R. Carpenterer, H.A. Tajmir-Riahi, Polyamine analogues bind human serum albumin, Biomacromolecules 8 (2007) 3177–3183.
[14] C.D. Kanakis, P.A. Tarassitin, H.A. Tajmir-Riahi, Polysialic acid-Polyamine analogues bind human serum albumin, Biomacromolecules 8 (2007) 970–977.
[15] C.N.N. Soukop-Koukis, R. Sedghat-Herati, C. Ragl, S. Hotchandani, H.A. Tajmir-Riahi, Retinol and retinoic acid bind human serum albumin: stability and structural features, Int. J. Biol. Macromol. 40 (2007) 484–490.
[16] M.A. Rub, J.M. Khan, N. Azum, A.M. Asiri, Aggregation and conformational stability evaluation of myoglobin in the presence of ionic surfactant, J. Mol. Liq. 241 (2017) 91–98.
[42] T. Yadav, D. Tikariha, J. Lakra, A.K. Tiwari, S.K. Saha, K.K. Ghosh, Surface properties of amphiphilic drugs in presence of cationic surfactants, J. Surface Sci. Technol. 30 (2014) 93–110.

[43] S. Sinha, D. Tikariha, J. Lakra, T. Yadav, S. Kumari, S.K. Saha, K.K. Ghosh, Interaction of bovine serum albumin with cationic monomeric and dimeric surfactants: A comparative study, J. Mol. Liq. 218 (2016) 421–428.

[44] C. Tesseromatis, A. Alevizou, The role of the protein-binding on the mode of drug action as well the interactions with other drugs, Eur. J. Drug Metabol. Pharmacokinet. 33 (2008) 225-230.

[45] J. Jin, J. Zhu, X. Yao, L. Wu, Study on the binding of farrerol to human serum albumin, J. Photochem. Photobiol. A: Chemistry 191 (2007) 59–65.

[46] A.N. Khramov, J.A. Stenken, Enhanced microdialysis recovery of some tricyclic antidepressants and structurally related drugs by cyclodextrin mediated transport, Analyst 124 (1999) 1027–1033.

[47] A. Sulkowska, Interaction of drugs with bovine and human serum albumin, J. Mol. Struct. 614 (2002) 227–232.

[48] S. Ghoudhary, N. Kirhore, Drug: protein interactions in micellar media: Thermodynamic aspects, J. Colloid Interface Sci. 431 (2014) 118–126.

[49] S. Mahajan, R.K. Mahajan, Interactions of phenothiazine drugs with bile salts: Micellization and binding studies, J. Colloid Interface Sci. 387 (2012) 194–204.

[50] U. Karaballi, S. Jaldappagari, S.S. Kalanur, Probing the binding of fluoxetine hydrochloride to human serum albumin by multispectroscopic, Spectrochim. Acta Mol. Biomol. Spectrosc. 75 (2010) 314–319.

[51] L. Galantini, C. Leggio, Human serum albumin unfolding: a small-angle x-ray scattering and light scattering study, J. Phys. Chem. B112 (2008) 15460–15469.