4.2 Nanoencapsulation of [60] fullerene by bis-β-cyclodextrin

4.2.1 Brief Review

Carbon allotropes are a class of promising nanomaterials that have many unique and fascinating physical, electrical and chemical properties[1-7]. Recent research on fullerenes, carbon nanotubes, carbon microcoils and graphene suggest that they can be functional for a number of applications such as in catalysis[8-15], solar cells[16], photosensitizers[17], superconducting materials[18], biosensors[19], hydrogen storage[20] etc, owing to their excellent electron affinity[21, 21] and charge transfer capabilities[23-25]. Among the commercially available carbon allotropes, a huge amount of literature is available on C_{60} apart from its exceptional biomedical applications owing to its DNA-cleaving, anti-HIV and radical scavenging activity[26-29]. C_{60} is soluble in many organic solvents and completely insoluble in water[30]. However, zero water-solubility of C_{60}, makes it quite challenging to use its properties in aqueous medium for biomedical applications[31, 32]. For most of the biomedical applications of C_{60}, organic solvents should be eliminated. Making a water-soluble C_{60} was also one of the great challenges in fullerene chemistry. While a number of fullerene derivatives have been prepared for such a purpose, most of them have been of poor or little aqueous solubility and less stability[33]. Therefore, preparation of a highly water-soluble C_{60} with superior stability in aqueous medium is a challenge. In search of an ideal system for the solubilization of C_{60}, non-covalent interactions of C_{60} with different biocompatible solubilizing agents such as surfactants, lysozyme, disaccharides and cyclodextrins has been reported[34-38]. Non-covalent inclusion complexation of C_{60} with macrocyclic cavitands such as cyclodextrins, calixarenes, curcubiturils, porphyrins, cyclotriveratrylene, has attracted attention of researchers to obtained water-soluble C_{60}[39, 40]. Among these macrocyclic cavitands, cyclodextrins are commercially available and biocompatible host molecules and widely utilized for the solubilization of C_{60} and other different hydrophobic molecules[41-45]. Even among the different cyclodextrins, initially it was believed that only γ-cyclodexrtrin with inner cavity size of 0.95 nm can form inclusion complex with C_{60} and α and β-cyclodextrins with inner cavity size 0.78 nm and 0.57 nm respectively, were ruled out for the formation of inclusion complex. But it seemed to be only experimental failures that were later overcome by adopting right experimental conditions that led to all three cyclodextrins to be able to form 2:1 inclusion complex

with C_{60}[46]. One drawback in using the inclusion complex of C_{60} with pristine cyclodextrins is that cyclodextrins have limited water-solubility and less stability (easily form agglomerates) in biological medium. Though β-cyclodextrin is cheapest among the three common cyclodextrins, the low water-solubility and cytotoxicity of the pristine β-cyclodextrin limits its further application in biomedical research[47, 48]. This drawback has stimulated a great deal of research to modify the β-cyclodextrin properties by selective conversion of hydroxyl groups to other functionalities. Thus a bis-β-cyclodextrin was synthesized having moderate water-solubility, inclusion ability and cytotoxicity[49].

There have been reports in literature on bridged bis-cyclodextrin as multifunctional receptors, which can selectively bind a wide variety of guest molecules through hydrophobic interactions, forming the stable host-guest inclusion complexes[50]. β-cyclodextrin dimer (bis-β-cyclodextrin) tethered by the small spacer (or linker) have different inclusion ability and solubility that can afford distinctly different binding abilities and molecular selectivity[51-53]. Therefore, in literature the diverse difunctional groups such as alkanedioates, disulfides, dipyridines, stilbene, and imidazole have been introduced as the linking agent to connect two cyclodextrin units[54, 55]. However, cyclodextrin dimers tethered with ethylenediamine units have been synthesized but their molecular recognition behavior with C_{60} is not known.

As a part of our ongoing research on solubilization of C_{60} in aqueous medium, herein we have report a facile way to prepare a water-soluble C_{60} by self-assembly of bis-β-cyclodextrin with C_{60} through non-covalent inclusion complexation. In 2005, Yu et al. reported the covalent conjugation of C_{60} on the α-methylene of 2,2'-bridged bis (β-cycodextrin)[56]. To the best of our knowledge this is the first report on non-covalent inclusion complex of C_{60} with bis-β-cyclodextrin, which is simple, effective and low-cost protocol for the aqueous solubilization of C_{60}. The structure, morphology and composition of the self-assembled inclusion complex was characterized by Fourier Transform Infrared Spectroscopy (FT-IR), UV-visible absorbance Spectroscopy (UV-vis), X-ray diffraction (XRD) and Thermogarvimetric analysis (TGA). The particle size of the inclusion complex was measured by Transmission Electron Microscopy (TEM) and Static Light Scattering (SLS) analyses.

4.2.2 Experimental

4.2.2.1 Materials

β-Cyclodextrin and C_{60} (purity > 99.9 %) were purchased from Sigma-Aldrich Co. β-Cyclodextrin was dried overnight under vacuum at 60^{o}C and used without further purification. The bis-β-cyclodextrin was synthesized as shown in Scheme 4.2.1 and characterized according to procedure described in literature[49]. Pyridine, N, N' dimethylformamide(DMF), ethylenediamine and toluene were purchased from Merck (Germany) and dried over calcium hydride for 24 hours and then distilled under reduced pressure before use.

4.2.2.2 Measurements

FT-IR spectra were taken on Shimadzu (8400S) instrument by KBr pellet method. UV-vis spectra of the solutions were recorded on a Shimadzu-2450 spectrophotometer. ^{1}H spectra were recorded on a JEOL JNM-LA300WB; 400 MHz instrument. *All spectra were measured in D_2O as solvent and the chemical shifts were referenced to tetramethylsilane (TMS) at 0 ppm.* XRD patterns were measured on a Rikagu diffractometer with CuKα radiation (λ = 0.154 nm) at 40 kV and 40 mA. TGA was made on a Shimadzu, TGA-50 system with a heating rate of 10 ^{o}C/min under air atmosphere in the temperature range of 30-700 ^{o}C. *To study the morphology and particle size of the inclusion complex, an energy-filtering transmission electron microscopy (TEM) [EF-TEM, EM 912 OMEGA (ZEISS, S-4700), 120 kV] was used. For TEM observation, the 1 % complex solution in double distilled water was drop casted on 400 mesh carbon-coated copper grids and annealed at 100 °C for 12 hours before measurement.* Particle size was measured by static light scattering technique with Ga-As semiconductor laser (mini Dawn Tristar, Wyatt). For the molecular modeling studies, the software ChemOffice 2004 (Chem 3D Ultra 8.0version) was used.

4.2.2.3 Synthesis of C_{60}-bis-β-cyclodextrin inclusion complex

The bis-β-cyclodextrin was synthesized as shown in Scheme 4.2.1 and characterized according to procedure described in literature[49]. The inclusion complex between C_{60} and bis-β-cyclodextrin were prepared by using a mixed solvent system to bring water-insoluble C_{60} and water-soluble bis-β-cyclodextrin into one homogeneous

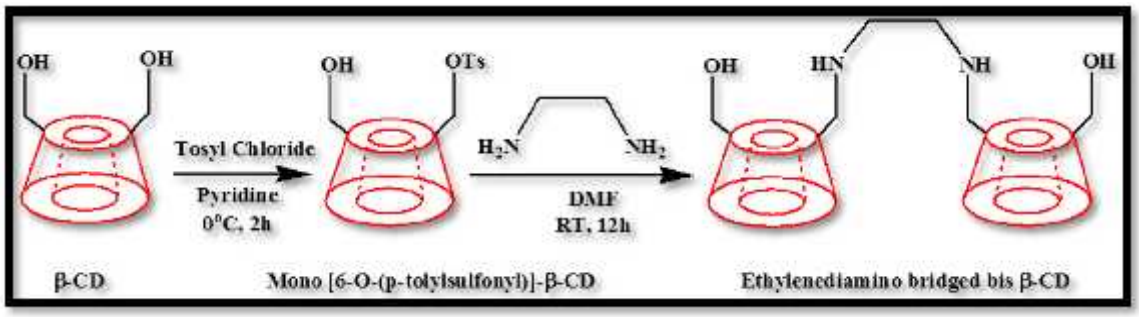
phase and shown in scheme 4.2.2. Thus, bis-β-cyclodextrin 1000 mg (0.440 mmoL) was dissolved in polar solvent DMSO and C_{60} 10 mg (0.014 mmoL) in the non-polar solvent toluene. These two solutions were mixed together and stirred for two days in nitrogen atmosphere at room temperature, during which the deep purple homogeneous solution turned deep brown. The progress of the reaction was monitored by taking an aliquot of the reaction mixture every 4h and measuring the UV absorbance. After the completion of the reaction, the reaction product was isolated by removing the organic solvent on a rotary evaporator under vacuum when a brown solid resulted. This was dissolved in excess of water under stirring. The insoluble material was removed by filtration through 0.45 µm syringe-filter. The filtrate was purified and concentrated by ultrafiltration over a polymer membrane (MWCO 1K) to remove uncomplexed bis-β-cyclodextrin. The concentrated aqueous solution was freeze-dried to get a brown colored product.

4.2.2.4 Determination of Stability Constant

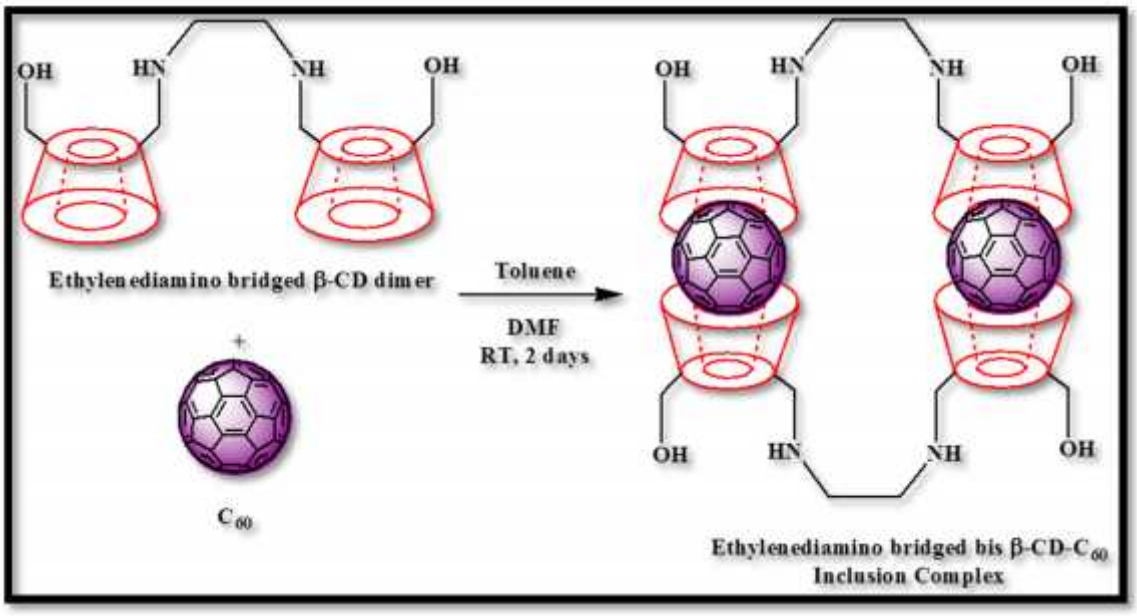
In order to determine the stability constant of the inclusion complex of bis-β-cyclodextrin and C_{60}, the concentration of the C_{60} was kept constant at $1x\ 10^{-3}$ mol dm^{-3} and the concentration of bis-β-cyclodextrin varied from $2 x 10^{-3}$ mol dm^{-3} to $10 x 10^{-3}$ mol dm^{-3}. The UV-vis absorbance of the aqueous solution at 348 nm was measured at these concentrations and the data fit to the Benesi-Hildebrand equation[57]. The best fit was obtained for the 2:2 complex of the bis-β-cyclodextrin/C_{60} inclusion complex. Based on this equilibrium, the Benesi-Hildebrand equation for a 2:2 complex is given by:

$$\frac{[G]^2}{A} = \frac{1}{K\varepsilon} \times \frac{1}{[H]^2} + \frac{1}{\varepsilon} \qquad (1)$$

Where [G] is the guest concentration, [H] is the host concentration, A is the absorbance of the guest, K is the equilibrium constant, and ε is the extinction coefficient for the absorbing species.



Scheme 4.2.1 Synthesis of ethylenediamno bridged bis-β-cyclodextrin.



Scheme 4.2.2 Synthesis of ethylenediamno bridged bis-β-cyclodextrin-C_{60} inclusion complex.

4.2.3 Results and Discussion

4.2.3.1. Aqueous Solubility

As expected, after dimerization there is a significant enhancement of the aqueous solubility of β-cyclodextrin from 18.4 $mgmL^{-1}$ to 27.0 $mgmL^{-1}$ at room temperature. The low aqueous solubility of parent β-cyclodextrin is attributed to the rigid structure, due to the intramolecular hydrogen bonding between the secondary hydroxyl groups and primary hydroxyl groups, which are unfavorable for the interaction between β-cyclodextrin and surrounding water molecules. The formation of bis-β-cyclodextrin disrupts the intramolecular hydrogen bonding and hydrated molecules of water from cyclodextrin escape, thus increasing the aqueous solubility. Moreover, it is also known that chemical modification of β-cyclodextrin changes the size and the shape of the cavity. For example, it has been reported that by methylation, the depth of the cavity is extended from 780 pm to 1100 pm and the hydrophilic nature of both ends of the β-cyclodextrin changes[58]. Thus, the improved water-solubility and inclusion ability of bis-β-cyclodextrin was used for the solubilization of C_{60}. The aqueous solubility of bis-β-cyclodextrin/C_{60} inclusion complex was measured and was found to be 16 $mgmL^{-1}$, which is four times higher than the reported water-solubility 4 $mgmL^{-1}$ of β-cyclodexrin/C_{60} inclusion complex[59].

4.2.3.2. Stability Constant

The most characteristic feature of the host-guest inclusion complex is its equilibrium in solution. The equilibrium constant, thus is the most essential measure of the stability of the inclusion complex. Different techniques have been used to study the cyclodextrin inclusion complex stability[59, 61]. Absorption spectroscopy is an excellent tool of estimating the inclusion complex stability constant, when the guest has typical absorption bands in solution[61]. The possible reaction between the bis-β-cyclodextrin and C_{60} is given in Scheme 4.2.2. From the measurement of the absorbance of the C_{60} in the inclusion complex at different concentrations of bis-β-cyclodextrin, and fitting the data to the double reciprocal plot the equilibrium constant, K, for the complex was calculated. It was found to be 1.78 x $10^6 M^{-1}$ and the extinction coefficient ε to be 4290 $cm^{-1}M^{-1}$ (Figure 4.2.1). From this result in connection with Eq. (1), it is evident that bis-β-cyclodextrin and C_{60} form a more stable 2:2 inclusion complex as compared to pristine β-cyclodextrin and C_{60} 2:1 inclusion complex in aqueous solution (Table 4.2.1).

4.2.3.3. Fourier Transform Infrared Spectroscopy (FTIR)

FT-IR spectra of bis-β-cyclodextrin, C_{60} and bis-β-cyclodextrin-C_{60} inclusion complex are shown in Figure 4.2.2. FT-IR spectrum of bis-β-cyclodextrin (Fig. 4.2.2a) showed the typical characteristic absorption bands of β-cyclodextrin at 3331 cm^{-1} (-OH stretching hydrogen bonded, NH stretching bond), 2930 cm^{-1} (C-H stretching), 1641 cm^{-1} (OH bending), 1365 (OH deformation), 1168 cm^{-1} (C-O-C stretching and OH bending), 1080 cm^{-1} and 1032 cm^{-1} for (C-O-C stretching). FT-IR spectrum of pristine C_{60} (Fig. 4.3b) shows four typical absorption peaks at 1429 cm^{-1}, 1183 cm^{-1}, 578 cm^{-1} and 527 cm^{-1}. Besides this the FT-IR spectrum of bis-β-cyclodextrin-C_{60} inclusion complex (Fig. 4.2.2c) shows all the typical characteristic absorption peaks of β-cyclodextrin, which was observed to be shifted along with the presence of typical absorption peaks of C_{60} at 578 cm^{-1} and 527 cm^{-1} and it is also observed that the β-cyclodextrin peaks remains strong in the spectrum. These results confirmed the formation of inclusion complex between bis-β-cyclodextrin and C_{60}[37].

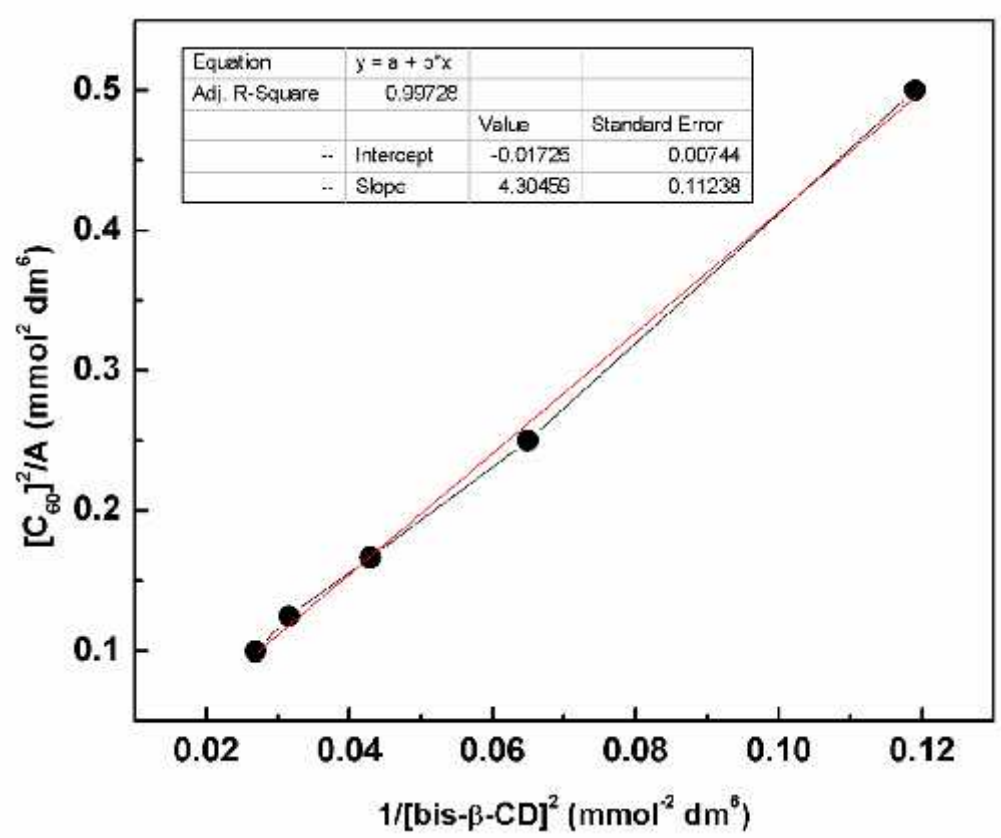


Figure 4.2.1 The double-reciprocal plot of the variation of absorbance at 348 nm at different bis-β-cyclodextrin concentrations and fixed concentration of C_{60}.

Table 4.2.1 Parameter Comparison for the β-Cyclodextrin-C_{60}, γ-Cyclodextrin-C_{60} andbis-β-cyclodextrin-C_{60}Inclusion Complexes in Aqueous Solution

Inclusion Complex	**Equilibrium Constant, K (dm^6 mol^{-2})**	**Extinction Coefficient, Ɛ ($dm^3mol^{-1}cm^{-1}$)**	**Reference**
Bis-(β-CD)/C_{60}	1.78 x 10^6	4290	This work
β-CD/C_{60}	1.69×10^5	2,050±100	55
γ-CD/C_{60}	2.6×10^7	12,200	56

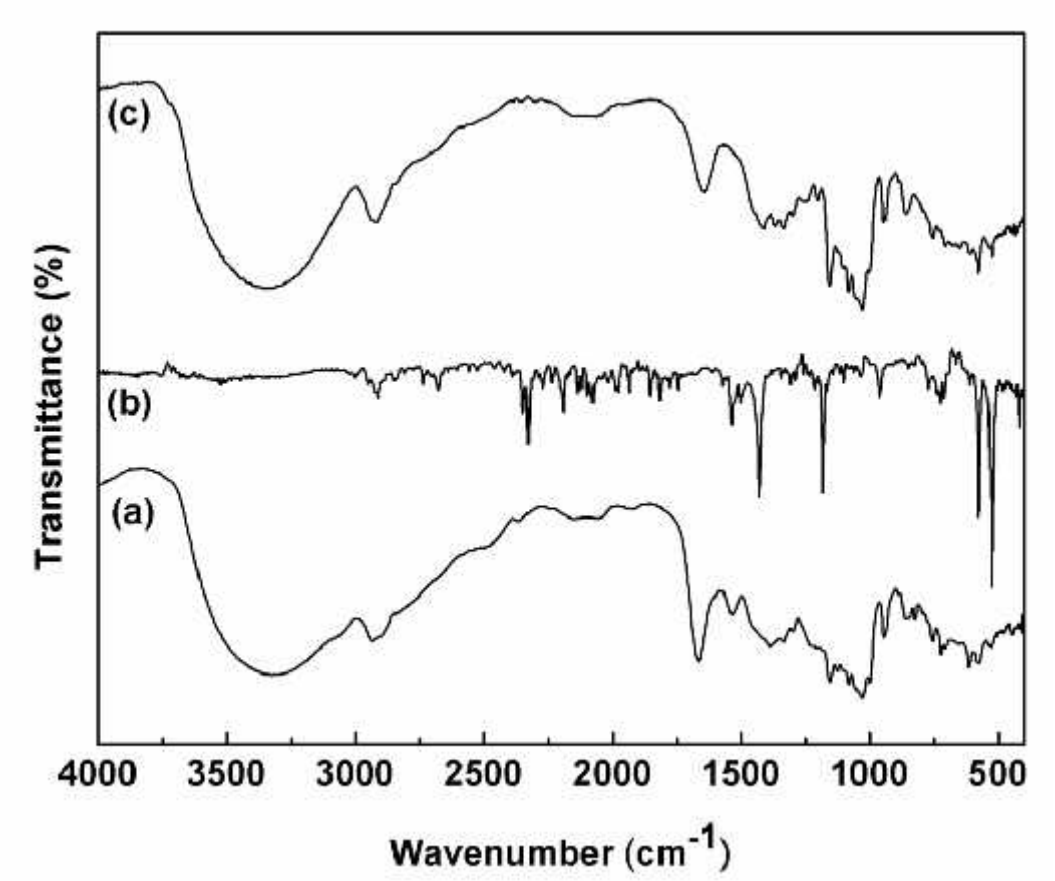


Figure 4.2.2 FT-IR spectra of (a) bis-β-cyclodextrin, (b) C_{60} and (c) bis-β-cyclodextrin-C_{60} inclusion complex.

4.2.3.4. UV-Vis Spectra

UV-Vis absorbance spectra of C_{60}, bis-β-cyclodextrin and bis-β-cyclodextrin-C_{60} inclusion complex are shown in Figure 4.2.3. UV-vis absorbance spectrum of C_{60} (Fig. 4.2.3a) shows absorbance maxima at 334 nm and typical peak at 407 nm in toluene; whereas UV-vis absorbance spectrum of bis-β-cyclodextrin in water (Fig. 4.2.3b) does not show any absorbance in this region. However, the UV-Vis absorbance spectrum of bis-β-cyclodextrin-C_{60} inclusion complex in water (Fig. 4.2.3c) shows the typical absorbance of C_{60} which is red shifted by 10 nm. Moreover, the peak broadening of the absorbance beyond 407 nm is assigned to the characteristic absorption of C_{60}. In order to understand the interaction between bis-β-cyclodextrin and C_{60}, an aqueous solution of bis-β-cyclodextrin-C_{60} inclusion complex was shaken with toluene for few minutes and the UV-Vis absorbance of aqueous phase and organic phase was recorded. The aqueous phase shows absorbance spectra similarly to that of bis-β-cyclodextrin-C_{60} inclusion complex in water whereas organic phase does not shows any absorbance. This suggests that the bis-β-cyclodextrin-C_{60} inclusion complex is stable enough and it was impossible to extract C_{60} from aqueous solution of inclusion complex.

4.2.3.5. Nuclear Magnetic Resonance Spectroscopy (NMR)

The type of interaction between C_{60} and bis β-CD was further confirmed by NMR spectra taken in D_2O. The ^1H NMR spectra of bis β-CD and bis β-CD/C_{60} inclusion complex in D_2O was shown in Figure 4.2.4. The ^1H NMR spectra of bis β-CD and bis β-CD/C_{60} inclusion complex shows the similar proton signal due to the similar hydrogen structure, except upfield shifts of some protons signal was observed. It is well known that protons at the H-3 and H-5 positions in D-glucose units upfield shifted by the encapsulation of the guest molecule in the inner hydrophobic cavity of β-CD. The upfield shifts of protons at the H-3 and H-5 position observed due to nanoencapsulation of C_{60} in inner hydrophobic cavity of the bis β-CD have been considered as an evidence for the formation of an inclusion complex. A similar observation was reported by several groups[34, 39, 60].

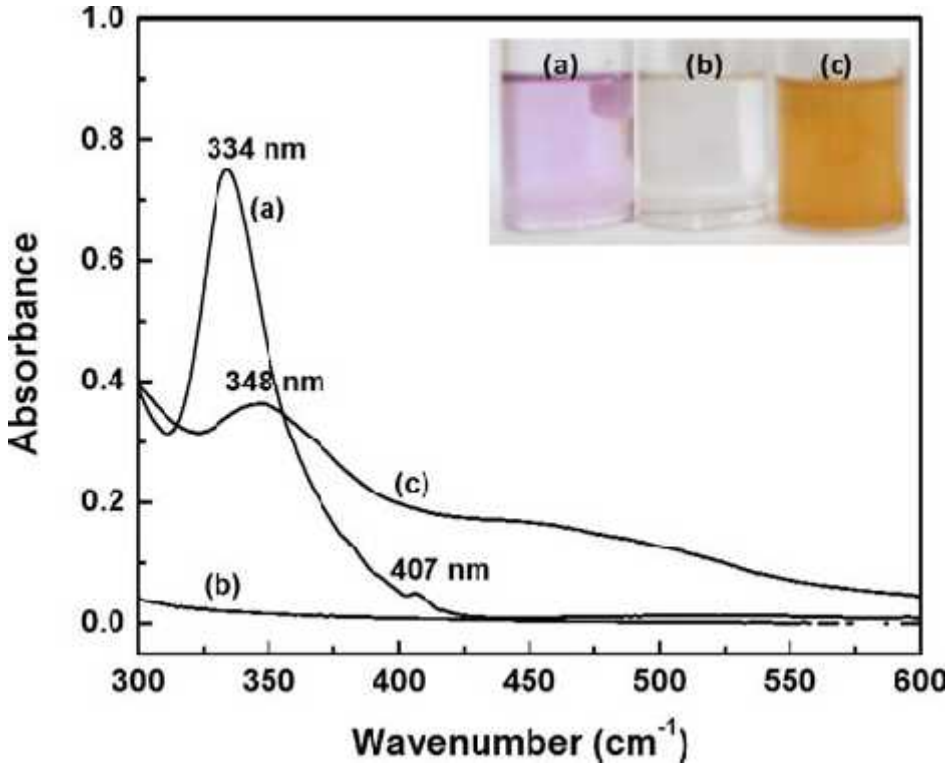


Figure 4.2.3 UV-vis absorbance spectra of (a) C_{60} in toluene, (b) bis-β-cyclodextrin in water and (c) bis-β-cyclodextrin-C_{60} inclusion complex in water.

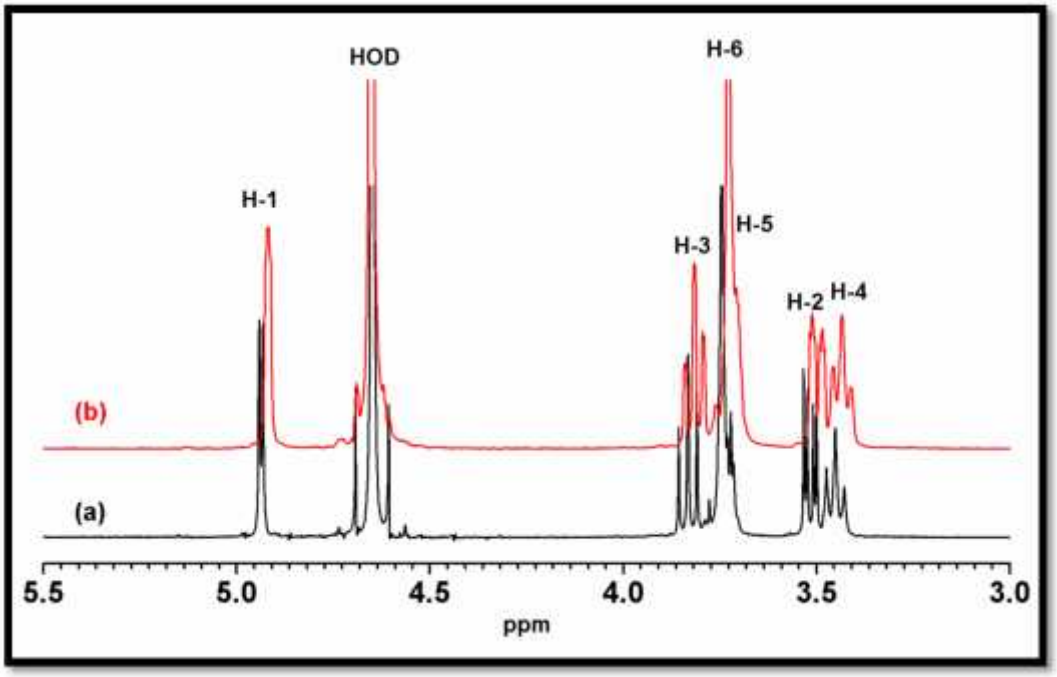


Figure 4.2.4 ^{1}H NMR spectra of (a) bis β-cyclodextrin and (b) bis β-cyclodextrin/C_{60} inclusion complex.

4.2.3.6. Thermogravimetric Analysis (TGA)

In order to further ascertain the stoichiometry and thermal stability of the bis-β-cyclodextrin-C_{60}, thermogravimetric analysis of reactants and products were investigated as shown in Figure 4.2.5. The bis-β-cyclodextrin-C_{60} inclusion complex shows three stage decomposition at elevated temperature. The first stage of weight loss is ascribed to the loss of hydrated water molecules. The second stage of weight loss is attributed to decomposition of glucose units of the bis-β-cyclodextrin. Therefore, the weight loss of the third stage is mainly caused by the decomposition of C_{60}. However, the formation of the assembly results in a remarkably early degradation of C_{60} (beginning from ~350 $^{\circ}$C) compared with pristine C_{60} (beginning from ~520 $^{\circ}$C). The theoretical calculated weight content of bis-β-cyclodextrin of 1:2 and 2:2 inclusion complex with C_{60} was found to be 61.45 % and 76.12 %, respectively. TGA curve of bis-β-cyclodextrin-C_{60} inclusion complex showed that the weight loss of the bis-β-cyclodextrin at ~327 $^{\circ}$C was 75.90 % [40]. This result indicates that there are two fullerene molecules sandwiched between every two bis-β-cyclodextrin molecules supporting the structure as shown in Scheme 4.2.2.

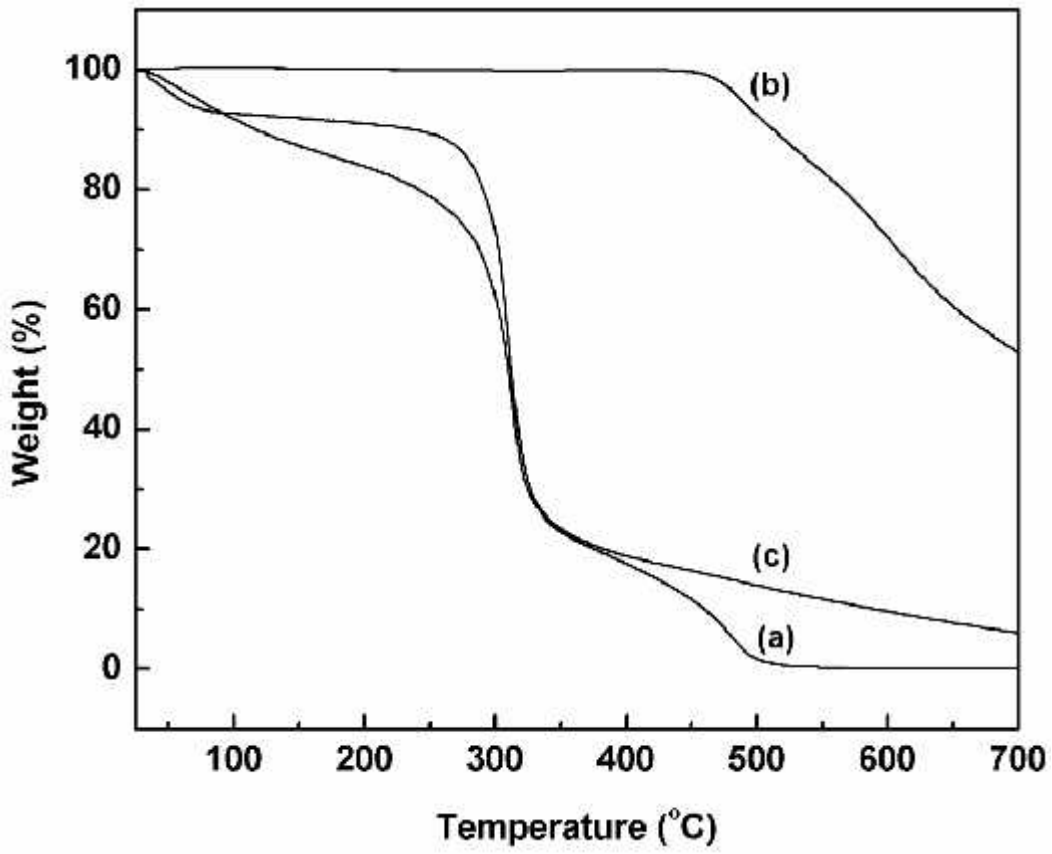


Figure 4.2.5 TGA curves of (a) bis-β-cyclodextrin-C_{60} inclusion complex, (b) C_{60} and (c) bis-β- cyclodextrin.

4.2.3.7. X-ray Diffraction (XRD)

More direct evidence for the formation of stable bis-β-cyclodextrin/C_{60} supramolecular assembly comes from X-ray diffraction studies. X-ray diffraction (XRD) is a generally used method to characterize cyclodextrin-based complexes and aggregates, because XRD patterns of the resulting complexes and aggregates should be different from those of native cyclodextrins. The X-ray diffraction pattern of the β-cyclodextrin, bis-β-cyclodextrin, C_{60} and freeze-dried bis-β-cyclodextrin-C_{60} are shown in Figure 4.2.6. The XRD pattern of free bis-β-cyclodextrin (Fig. 4.2.6b) displaying three broad bands below 25^o clearly indicates the slight amorphous nature of free bis-β-cyclodextrinas compared to the crystalline peaks of the parent β-cyclodextrin (Fig. 4.2.6a) owing to the loss of hydrated water molecules during the formation of dimer. C_{60} (Fig. 4.2.6c) shows diffraction peaks at 2θ = 10.7^o, 17.6^o, 20.7^o, 21.6^o, 27.3^o, 28.0^o, 30.7^o, 32.7^o. In contrast, the XRD pattern of bis-β-cyclodextrin-C_{60} inclusion complex, unambiguously (Fig. 4.2.6d) shows different from parent of β-cyclodextrin and bis-β-cyclodextrin, but resembles that of C_{60}, exhibiting several sharp reflections at 2θ= 10.9^o, 17.8^o, 21.0^o, 28.7^o, 31.5^o, 33.7^o which are assigned to (111), (220), (311), (420) and (333) planes of C_{60}[62,63]. These results indicate the inclusion of C_{60} in bis-β-cyclodextrin forming supramolecular self-assembled structure.

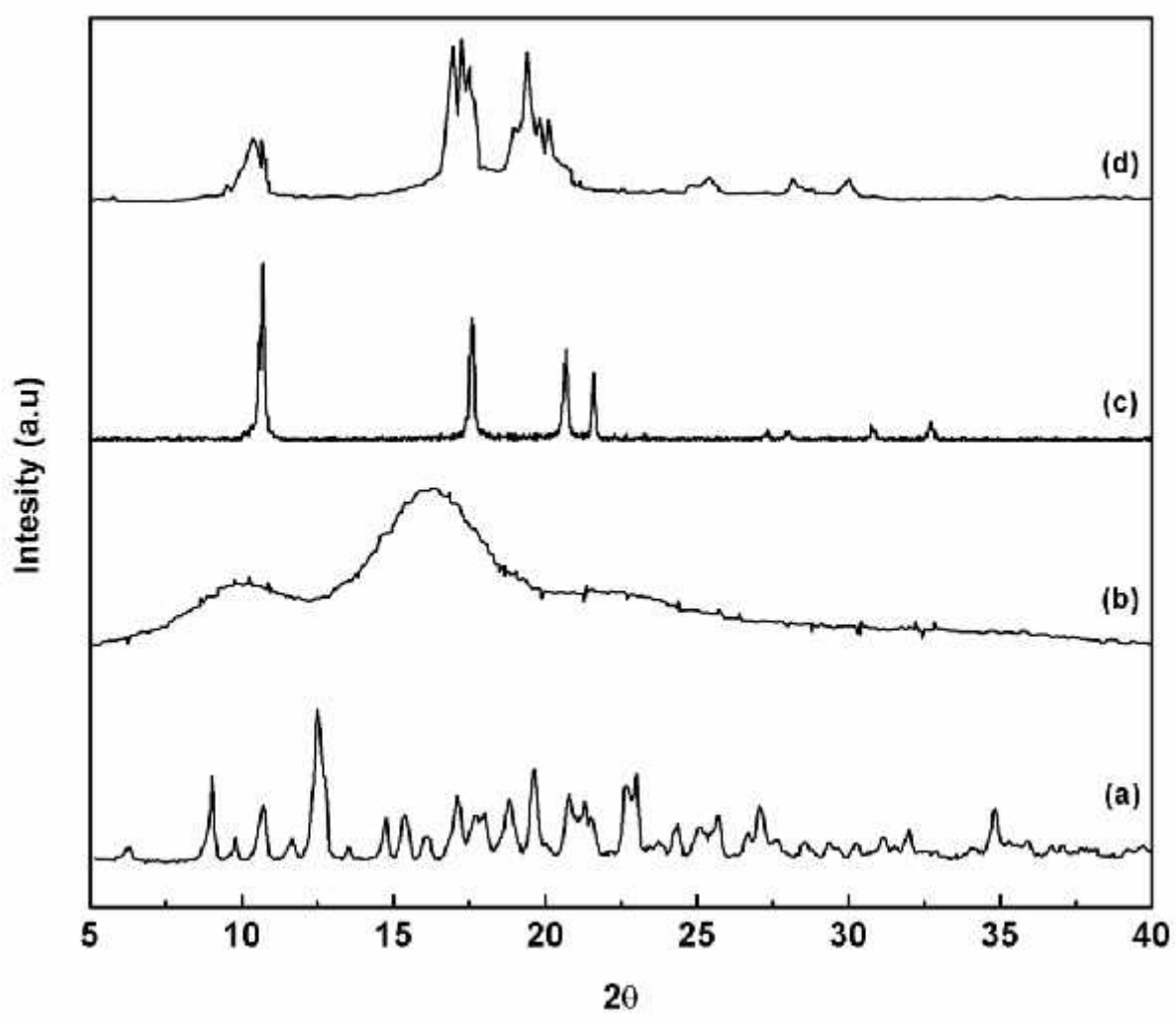


Figure 4.2.6 XRD difractogram of (a) β-cyclodextrin, (b) bis-β-cyclodextrin, (c) C_{60} and (d) bis-β-cyclodextrin-C_{60} inclusion complex.

4.2.3.8. Transmission Electron Micrograph (TEM) and Static Light Scattering (SLS)

The retention of the crystalline nature of the inclusion complex was further confirmed by TEM image as shown in Figure 4.2.7(a). The inclusion complex was found to have spherical shape with uniform crystalline aggregates of about 30±5 nm. The particles size obtained from static light scattering (SLS) measurements also support the prior inference drawn from TEM micrographs. Even though the concentration of inclusion complex in aqueous solution was increased, the particle size does not change and was found to be 30±5 nm. High resolution TEM (HR-TEM) image (Fig. 4.2.7(a), Inset) shows a crystal lattice of the C_{60} with bis-β-cyclodextrin with the lattice spacing between the fullerene molecules of the order of 0.34 nm (Fig.4.2.7(c)). This is similar to the lattice spacing between the C_{60} crystal planes in the solid state. Moreover, the bis-β-cyclodextrin-C_{60} inclusion complex shows unique spherical self-assembly as shown in Figure 4.8(b) due to the non-covalent integrations such as van der Waals forces, hydrogen-bonding, hydrophilic/hydrophobic interactions, π-π stacking interaction, electrostatic interactions, donor and acceptor interactions, etc.

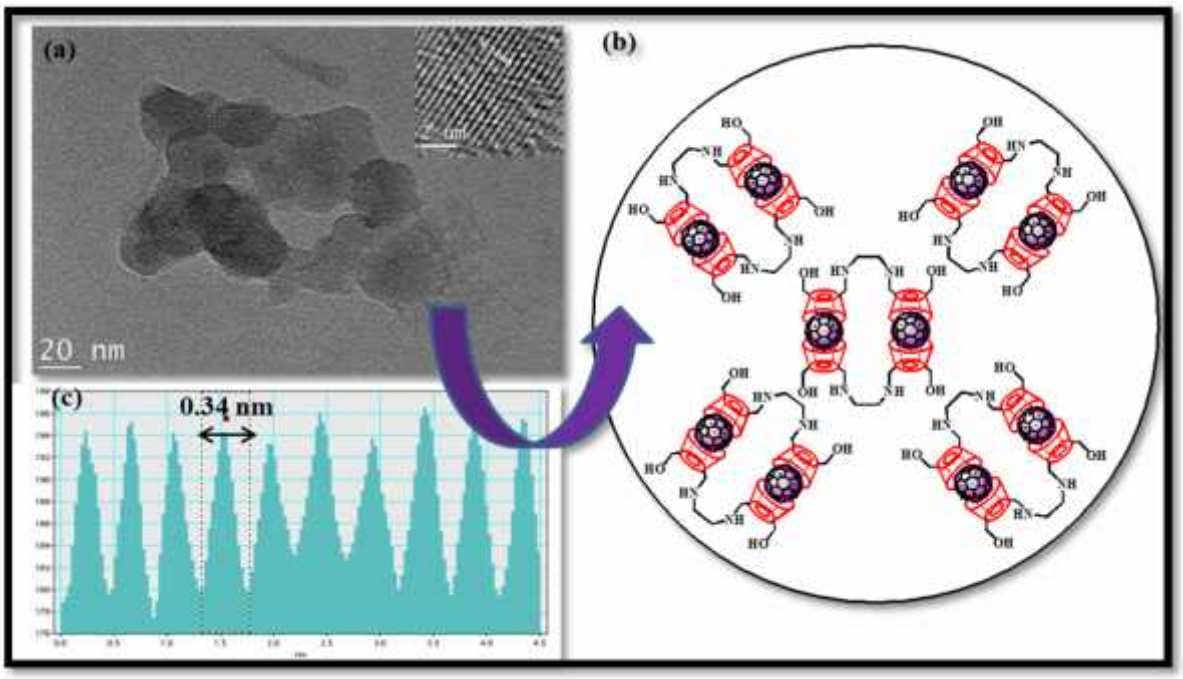


Figure 4.2.7 (a) TEM micrograph of bis-β-cyclodextrin-C_{60} inclusion complex; Inset: HRTEM image of C_{60} lattice (b) spherical self-assembly of bis-β-cyclodextrin-C_{60} inclusion complex (c) histogram showing the lattice spacing of 0.34 nm.

4.2.4 Conclusions

Successfully prepared a novel inclusion complex of poorly water-soluble antibiotic drug cefpodoxime proxetile (CPDX) and antiepileptic drug carbamazepine (CBZ) with β-CD and β-CD based polymers, so as to improve water-solubility and biocompatibility in aqueous medium. The results show that the inclusion complex is of 1:1 type. Interestingly it was found that the β-CD based polymers considerably enhance the water-solubility of CPDX and CBZ as compared to the pristine β-CD. It is also worthwhile to mention here that the solubility was enhanced seven times higher than the intrinsic water-solubility of drugs in presence of β-CD based polymers.

Bis-β-cyclodextrin was synthesized to improve water-solubility, and moderate inclusion ability of parent β-cyclodextrin. The bis-β-cyclodextrin can easily form self-assembled inclusion complex with C_{60}, having higher water-solubility and stability than the typical 2:1 inclusion complex of β-cyclodextrin/C_{60}. The stability constant was determined from Bensi-Hildebrand equation and absorbance studies are found to be 1.78×10^6 M^{-1}. The stoichiometry of inclusion complex was found to be 2:2 determined from Benesi-Hildebrand plot and TGA analysis. The particle size of the self-assembly was found to be 30±5 nm from TEM and SLS measurements. This adduct has potential biomedical applications, work in this direction to use this adduct for DNA-cleaving and as radical scavenger is in progress.

References

1. B. Narymbetov, A. Omerzu, V.V. Kabanov, M. Tokumoto, H. Kobayashi, D. Mihailovic, *Nature*., **2000**, 407, 883-885.
2. T. L. Makarova, B. Sundqvist, R. Hohne, P. Esquinazi, Y. Kopelevich, P. Scharff, V.A.L. Davydov, S. Kashevarova, A. V. Rakhmanina, *Nature.*, **2001,** 413, 716-718.
3. S. Ijima, *Nature*., **1991**, 345, 56-58.
4. P. M. Ajayan, S. Lijima, *Nature*, **1993**, 361, 333-334.
5. P. Calvert, *Nature.*,**1992**, 357, 365-366.
6. A.F. Hebard, M. J. Rosseinsky, R.C. Haddon, D. W. Murphy, S. H. Glarum, T. T. M. Palstra, A. P. Ramitez, A. R. Kortan, Nature., **1991**, 350, 600-601.
7. E. P. Grant, *Nature.,* **2001**, 413, 264-265.
8. D. R. Dreyer, C. W. Bielawski, *Chem. Sci.*, **2011,** 2, 1233-1240.
9. J. Pyun, *Chem. Inter. Ed*., **2011,** 50, 46-48.
10. D. R. Dreyer, C.W. Bielawski, Angew. *Chem. Inter. Ed*., **2010**, 49, 6813-6816.
11. J. Zhang, D. S. Su, A. H. Zhang, D. Wang, R. Schlogl, C. Hebert, *Angew. Chem. Inter. Ed.*, **2007**, 46, 7319-7323.
12. B. Frank, J. Zhang, R. Blume, R. Schlogl, S. D. Su, *Angew. Chem. Inter. Ed*., **2009**, 48, 6913-6917.
13. A. J. Zhang, S. D. J. Su, R. Blume, R. Schlogl, R. Wang, GX. Yang, A. Gajovic, *Angew. Chem. Inter. Ed*., **2010**, 49, 8640-8644.
14. B. Frank, R. Blume, A. Rinaldi, A. Trunschke, R. Schlogl, Angew. *Chem. Inter. Ed*., **2011**, 50, 10226-10230.
15. D. R. Dreyer, K. A. Jarvis, P. J. Ferreira, C. W. Bielawski, Macromolecules., **2011**, 44, 7659-7667.
16. A. L. Ayzner, D. D. Wanger, C.J. Tassone, S.H. Tolbert, B. J. Schwartz, *J. Phys. Chem. C*., **2008**, 112, 18711-18716.
17. C. Thilgen, F. Diederich, *Chem. Rev*., **2006**, 106, 5049-5135.
18. K. Yakigaya, A. Takeda, Y. Yokoyama, S. Ito, T. Miyazaki, T. Suetsuna, H. Shimotani, T. Kakiuchi, H. Sawa, H. Takagi, K. Kitazawa, N. Dragoe, *New J. Chem*., **2007**, 31, 973-979.
19. P. Alivisatos, *Nat. Biotechnol*., **2004**, 22, 47-52.
20. M. Yoon, S. Yang, E. Wang, Z. Zhang, *Nano Lett*., **2007**, 7, 2578-2583.

21. S. Bhattacharya, S. K. Nayak, A. Semwal, S. Chattopadhyay, M. Banerjee, *J. Phys. Chem. A*., **2004**, 108, 9064-9068.
22. P. D. W. Boyd, C. A. Reed, *Acc. Chem. Res*., **2005**, 38, 235-242.
23. O. O. Adisa, B. J. Cox, J. M. Hill, *Nano Lett*., **2010**, 5, 291-295.
24. J. Zhao, A. Buldum, J. Han, J. P. Lu, Nanotechnology., **2002**, 13, 195-200.
25. J. Zhang, T. Fuhrer, W. Fu, J. Ge, D. W. Bearden, J. Dallas, J. Duchamp, K. Walker, H. Champion, H. Azurmendi, K. Harich, H. C. Dorn, *J. Am. Chem. Soc.*, **2012**, 134, 8487-8493.
26. N. Gharbi, M. Pressac, M. Hadchouel, H. Szwarc, S. R. Wilson, F. Moussa, *Nano Lett*., **2005**, 5, 2578–2585.
27. L. Xiao, H. Takada, K. Maeda, M. Haramoto, N. Miwa, *Biomed. Pharmacother*., **2005**, 59, 351-358.
28. S. Samal, K. E. Geckeler, *Macromol. Biosci*., **2001**, 1, 329-331.
29. K. E. Geckeler, S. Samal, *Full. Sci. Techn*., **2001**, 9, 17-23.
30. M. A. Correa-Duarte, N. Wagner, J. Rojas-Chapana, C. Morsczeck, M. Thie, M. Giersig, *Nano Lett*., **2004**, 4, 2233-2236.
31. K. N. Semenov, N. A. Charykov, J. Chem. Eng. Data., **2010**, 55, 2373-2378.
32. B. S. Harrison, A. Atala, *Biomaterials*., **2007**, 28, 344-353.
33. A. Arrais, E. Diana, *Fullerenes, Nanotubes and Carbon NanostructuresFullerenes, Nanotubes, and Carbon Nanostructures.*, **2003**, 11, 35-46.
34. C. N. Murthy, K. E. Geckeler, *Chem. Commun*., **2001**, 3, 1194-1195.
35. C. N. Murthy, R. R. Patel, R. Murali, A. K. Rakshit, *J. Chem. Eng. Data*., **2010**, 55, 4479-4484.
36. V. I. Bhoi, S. Kumar, C. N. Murthy, *Carbohydr. Res*., **2012**, 359**,** 120-127.
37. V. I. Bhoi, C. N. Murthy, *Fullerenes, Nanotubes, and Carbon Nanostructures*., **2011**, 19, 668-676.
38. C. R. Prabha, R. Patel, C. N. Murthy, *Fullerenes, Nanotubes and Carbon Nanostructures*., **2004**, 12, 405-412.
39. T. Andersson, K. Nilsson, M. Sundahl, G. Westman, O. Wennerstrom, *Chem. Commun*., **1992**, 604-606.
40. D. D. Zhang, J. W. Chen, Y. Yang, R. F. Chai, X. L. Shen, *J. Incl. Phenom. Macrocycl. Chem*.,**1993**, 16, 245-253.
41. S. Samal, K. E. Geckeler, *Chem. Commun*., **2000**, 13, 1101-1102.
42. S. Samal, B. J. Choi, K. E. Geckeler, *Chem. Commun*., **2000**, 1373-1374.

43. D. Nepal, S. Samal, K. E. Geckeler, *Macromolecules.*, **2003,** 36, 3800-3802.
44. D. B. Y. Abdulilah, N. F. Al-Rawashdeh, I. Al-Momani, J. Incl. Phenom. *Macrocycl. Chem*., **2009**, 63, 109-115.
45. A. D. Abdulilah, N. Al-Rawashdeh, *J. Incl. Phenom. Macrocycl. Chem*., **2008,** 60, 293-301.
46. Y. Zhang, W. Liu, X. Gao, Y. L. Zhao, M. Zheng, F. F. Li, D. L. Ye, *Tetrahedron Lett*., **2006,** 47, 8571-8574.
47. Y. Ohtani, T. Irie, K. Uekama, K. Fukunaga, J. Pitha, *Eur. J. Biochem*., **1989**, 186, 17-22.
48. R. A. Rajewski, G. Traiger, J. Bresnahan, P. Jaberaboansari, V. J. Stella,D. O. Thompson, *J. Pharm. Sci*., **1995**, 84, 927-932.
49. B. Tang, H. L. Liang, L. L. Tong, P. Li, *Med. Chem*., **2006**, 3947-3952.
50. M. Narita, J. Itoh, T. Kikuchi, F. Hamada, *J. Incl. Phenom. Macrocycl. Chem*., **2002**, 42,107-114.
51. Y. Liu, Y. Li, H. Y. Zhang, X. Dong, *J. Org. Chem*., **2003**, 68, 527-536.
52. R. Breslow, S. Halfon, B. Zhang, *Tetrahedron*., **1995**, 51, 377-388.
53. P. Kuad, A. Miyawaki, Y. Takashima, H. Yamaguchi, A. Harada, *J. Am. Chem. Soc*., **2007**, 129, 12630-12631.
54. R. Breslow, N. Greenspoon, T. Guo, R. Zarzycki, *J. Am. Chem. Soc*., **1989**, 111, 8296-8297.
55. R. Breslow, S. Chung, *J. Am. Chem. Soc*., **1990**, 112, 9659-9660.
56. L. Yu, L. Peng, C. Yong, Z. Yan-Li, D. Fei, Y. Ao, *J. Phys. Chem. B*., **2005**, 109, 23739-23744.
57. H. A. Benesi, J. H. Hildebrand, *J. Am. Chem. Soc*., **1949**, 71, 2703-2707.
58. J. J. Stezowski, K. H. Jogun, E. Eckle, K. Bartels, *Nature*., **1978**, 274, 617-619.
59. C. N. Murthy, K. E. Geckeler, *Fullerenes, Nanotubes and Carbon Nanostructures*., **2002**, 10, 91-98.
60. K. I. Priyadarsini, H. Mohan, A. K. Tyagi, J. P. Mital, *J. Phys. Chem*., **1994**, 98, 4756-4759.
61. K. A. Connors, John Wiley: New York, **1987**, Ch., 8
62. C. N. Field, P. A. Hamley, J. M. Webster, D. H. Gregory, J. J. Titman, M. Poliakoff, *J. Am. Chem. Soc*., **2000**, 122, 2480-2488.
63. E. Bae, B. K. Kwak, W. S. Kim, Y. Kim, K. Choi, J. Yi, *J. Nanosci. Nanotechnol*., **2011**, 11, 3516-3522.