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ORIGINAL ARTICLE

Interaction of naproxen with β-cyclodextrin and its derivatives/polymer: experimental and molecular modeling studies

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Abstract The interaction of naproxen with β-cyclodextrin and its derivatives (hosts) as well as polymer has been studied using UV Visible (UV–Vis), Fourier Transform Infrared (FTIR), Nuclear Magnetic Resonance (NMR) spectroscopy and Scanning electron microscopy (SEM). In this paper, the solid inclusion complexes were prepared by freeze drying method. The formation constants of the complexes were determined by UV–Vis method. The adsorption properties of naproxen with β-Cyclodextrin bonded silica stationary phase (CDS) were studied for an in-depth understanding of the host–guest interaction. The inclusion process involving naproxen and hosts was investigated by using the PM3 quantum–mechanical semiempirical method. The stabilization energy values obtained from the semiempirical calculation showed the same relation with the formation constant values determined by UV–Vis spectroscopy.

Keywords β-Cyclodextrin · Inclusion complex · Formation constant · Naproxen · Stabilization energy

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Introduction

Cyclodextrins (CDs) are a well-known group of water-soluble macromolecules, which form inclusion complexes with a great variety of guest molecules. This property of forming inclusion complex with various guest molecules with suitable polarity and dimension is attributable to their special molecular structure—hydrophobic internal cavity and hydrophilic external surface [1, 2]. Several weak forces, including van der Waals, hydrophobic, dipole–dipole, and hydrogen bonding interactions, cooperatively determine the inclusion complex behaviour of the CD host [3, 4]. Thus CDs have been widely used in pharmaceutical industry [5], foodstuff [6, 7], separation technique [8, 9], environmental protection [10, 11], and so on.

β-Cyclodextrin (β-CD) is a cyclic oligosaccharide with seven glucose units, with its cavity structure, and can host a wide number of chemical compounds especially of pharmaceutical interest. The chemical structure of β-CD is shown in Fig. 1a. Although inclusion complex formation of β-CD with drugs has been extensively studied, because of its lower solubility, to some extent, its use was limited. However its solubility can be increased using, e.g., aqueous organic solvents (methanol or ethanol, below 30%), high pH, urea as a BGE modifier [12, 13], the wide number of β-CD derivatives etc. These chemically modified CDs have gained importance because of their relatively flexible cavity sizes, greater water solubility or less toxicity [14, 15]. Apart from parent CDs that have been extensively studied despite its low aqueous solubility, its alkylated derivatives, e.g. 2-hydroxy propyl-β-CD, have also attracted growing interest due to their improved complexing ability, greater water solubility and less toxicity [16].

Because of the diverse applications of CDs, during the past several decades considerable efforts have been

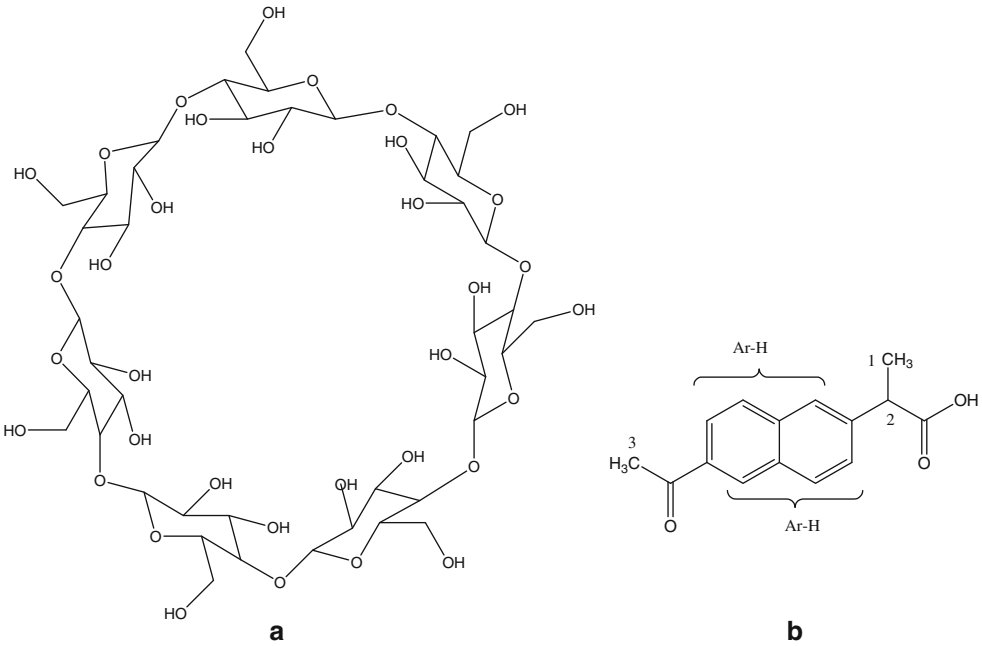

Fig. 1 Chemical structure of **a** β-CD and **b** naproxen

devoted to Cyclodextrin (CD) chemistry. Many experimental methods such as UV–Visible (UV–Vis), Fourier Transform Infrared (FTIR), fluorescence, circular dichroism, calorimetry, and Nuclear Magnetic resonance (NMR) have been developed to study the complexation behaviours of native and functionalized CDs [17, 18]. In order to get a better understanding of the binding events, a lot of theoretical methods [19] including molecular mechanics (MM) [20, 21], molecular dynamics [22] and quantum mechanics (QM) [23] methods, have also been used to study the CD complexes.

Naproxen is a poorly water soluble anti-inflammatory drug, the solubility of which can be enhanced by complexation with β-CD. Besides that, the inclusion complex reduces the incidence of gastrointestinal side effects of the drug [24]. Various analytical methods are used to determine naproxen in the presence of CDs, including UV–Vis detection [25–27], fluorimetry [28], NMR [29] and ion-selective electrodes [30]. The investigation on the properties, such as the interaction energy, preparation analysis, spectral property, adsorption equilibrium and kinetics, of naproxen with β-CD as well as its derivatives and polymers, will be important and significant not only in academics but also in industrial applications.

In this paper we report both experimental and theoretical studies on interactions of naproxen with β-CD/derivatives and polymer with emphasis on understanding the host–guest interaction. Adsorption behaviour of naproxen with β-CD bonded to silica gel has also been studied. Experimental methods along with theoretical ones will facilitate the understanding of the structural, energetic, and dynamic problems associated with CD complexes.

Materials and experimental methods

The naproxen used in this study was obtained from Sigma-Aldrich Chemicals Pvt. Ltd. USA. The molecular structure of naproxen is also shown in Fig. 1b. The β-CD was obtained from HiMedia Laboratories Pvt. Ltd., Mumbai, India. Other β-CDs used in this work such as β-CD hydrate (β-CD Hyd), 2-hydroxypropyl-β-CD (HP-β-CD) and β-CD-sulphated sodium salt (S-β-CD) were obtained from Sigma-Aldrich Chemicals Pvt. Ltd. USA. The silica gel (60–120 mesh size) was obtained from SRL Pvt. Ltd., Mumbai, India. This particular silica gel was chosen because of its highly porous structure and its appropriate physical and chemical properties needed to achieve both adequate loading and high binding capacities. Moreover, it is an efficient adsorbent for the separation of organic compounds by chromatographic methods. Compound 3-Glycidoxypropyltrimethoxysilane was also obtained from Sigma-Aldrich Chemicals Pvt. Ltd. USA. The other reagents used as components in buffers (sodium phosphate, sodium acetate, sodium carbonate and sodium chloride) were supplied by Qualigens, India (Mumbai) and were of analytical grade.

UV–Vis spectroscopy

The UV–Vis spectra were recorded with a Varian Cary 50 Bio (Sweden) UV–Vis Spectrophotometer using quartz cells, between 200 and 400 nm. In the experiments of naproxen (guest) with β-CD and its derivatives (hosts), the concentration of the hosts were varied from 1×10^{-3} M to 12×10^{-3} M while the concentration of the guest was kept constant at 2×10^{-3} M. The mixtures were stirred at

25 °C at a speed of 280 rpm for 4 h and the supernatant was analysed by UV–Vis spectrophotometer.

Preparation of drug-CD inclusion complexes powder

The guest and the hosts were fully dissolved in phosphate buffer (pH 8) at a molar ratio 1:1 and then the two solutions were mixed and stirred at 25 °C for 4 h. Dried complexes were obtained by lyophilisation in a freeze dryer where samples were frozen at −49 °C for 6 h followed by drying at 0.002 mbar for 12 h. The powders obtained were stored in gas-tight bottles at −20 °C until further analysis.

Instrumental studies

NMR spectra were recorded on a Varian 400 MHz NMR machine using D_2O and $CDCl_3$ as solvents. FTIR spectra were obtained by the KBr method (PerkinElmer, model Spectrum One). Morphological features of samples were obtained with a (Zeiss Sigma) Scanning Electron Microscope.

Preparation of β-CD bonded silica stationary phase (CDS)

CDs are highly soluble in water; thus, they must be processed into a solid form before utilisation in adsorption technologies. CD containing polymers are useful materials for selective adsorption or the separation of organic compounds. Therefore, a polymer (i.e., CDS) was synthesised as reported in earlier work [31] in which β-CD was bonded to silica particles.

CDS was prepared according to a previously reported procedure [32, 33]. Briefly, 1.145 gm of β-CD was dissolved in 25–30 ml of dry dimethyl formamide (DMF), to which 0.1 gm of metal sodium was added. The reaction was allowed to proceed with stirring at room temperature for approximately 30–40 min. After filtration, 0.45 ml of 3-Glycidoxypropyltrimethoxysilane was added to the filtrate, which is allowed to react at 90 °C for 5 h. Then, 5.0 gm of silica gel was added, and the mixture was allowed to react for 10 h at 80–100 °C. The CDS was filtered, and washed with DMF, methanol, doubly distilled water and acetone in sequence. Subsequently, the CDS was dried at 120 °C for 3 h, and kept in a desiccator before use.

Equilibrium isotherms and adsorption rate

Equilibrium isotherm was obtained by contacting 25 ml of aqueous naproxen solution with different amounts of CDS in a thermostated shaker bath controlled at 25 ± 0.5 °C at pH 8. The pH of the solutions were measured with a pH meter and maintained at pH 8 by using phosphate buffer reagents of appropriate dosages. The initial concentration of naproxen in the aqueous solution was varied between 5 and 10 mM. The equilibration time was 3–4 h. After attaining equilibrium, the aqueous phase was analysed for solute concentrations of the naproxen by a UV–Vis spectrophotometer (Varian Cary 50 Bio, Sweden) calibrated at the maximum absorbance wavelength (λ_{max}) of the specific naproxen. For quantitative spectrophotometric analysis, standard graph was prepared at λ_{max} 261 nm for naproxen. Approximately 0.2 mL of the supernatant liquid was drawn with glass syringe and diluted with the buffer used for preparing the naproxen solution. The absorbance was measured in the spectrophotometer and concentrations were determined using the calibration graph. The UV–Vis analysis was performed in duplicate and the reproducibility was found to be ±2%. The amount of naproxen per gram of CDS 'q' (mmol g^{-1}) was calculated as $q = V\Delta C/W$ where, ΔC is the change in solute concentration (mmol L^{-1}), V is the solution volume and W is the weight of adsorbent (g).

Molecular modeling studies

The inclusion process involving guest and hosts was investigated by using the PM3 quantum–mechanical semiempirical method. All theoretical calculations were performed using GAUSSIAN 09 software package [34]. For all the systems, a full geometry optimization was done at the PM3 level. Using standard bond lengths as the initial input, the carbon chains or rings in the guest molecule was vertically inserted into the cavity of the hosts along the middle axis from the large rim of hosts in CHEM 3D. Stabilization energy (ΔE) upon complexation between guest and the hosts were calculated for the minimum energy structure according to Eq. 1 [35]

$$\Delta E = E_{\text{complex}} - (E_{\text{guest}} + E_{\text{host}}) \quad (1)$$

where E_{complx}, E_{guest} and E_{host} represent HF energies (heats of formation) of the complex, the free naproxen and the host, respectively.

Results and discussion

UV–Vis spectroscopic studies

UV–Vis spectrophotometric studies of the interactions of guest with hosts enabled the determination of stability constants of inclusion complexes when their formation gave rise to appreciable spectral changes. The absorption spectrum of free naproxen showed only one peak with maximum at 228.5 nm and four other absorption peaks at 261 nm, 268.5 nm, 316 nm and 328.5 nm (Fig. 2). The

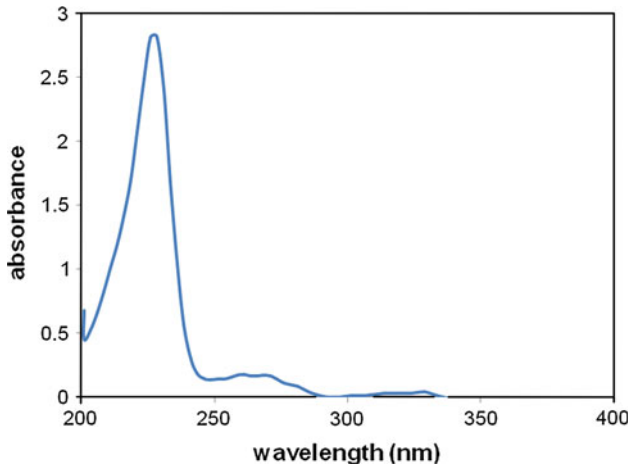

Fig. 2 UV absorption spectra of naproxen

UV–Vis spectrum of naproxen in phosphate buffered saline, described by Moore et al. [36], showed four absorption bands with maxima at 230 nm, 270 nm, 320 nm, and 330 nm, while Sobczuk et al. [37] had reported four peaks with maxima 262 nm, 271 nm, 317 nm and 330 nm. Typical UV–Vis absorption spectra of naproxen upon addition of β-CD, HP-β-CD, β-CD-Hyd and S-β-CD in aqueous solution at 298 K are shown in Fig. 3a, b, c, d, respectively. Upon addition of hosts the absorptivity increased in each case and the increase was significant with higher added concentration. Cyclodextrins strongly affected the absorptivity of the guest and therefore, the peak at 228.5 nm in the spectrum of guest was not prominent upon complexation with hosts other than S-β-CD. Analysing the spectra pertaining to naproxen-S-β-CD (Fig. 3d), at λ_{max} = 261 nm (in the spectra of the guest), showed that the peak shifted to 256 nm while in the other cases it remained almost unchanged which indicated that among the studied hosts, S-β-CD was better complexing agent for naproxen. The shifts towards lower wavelength in the spectra of the complexes may be attributable to the formation of hydrogen bonds. Because hydrogen bonding lowers the energy of 'n' orbitals, a hypsochromic shift (blue shift) was observed [38]. The shift was more pronounced in case of complexes with S-β-CD, which may be due to the greater affinity of sulphated oxygen towards hydrogen bonding [39].

Determination of formation constants of the inclusion complexes of hosts with guest

The determination of formation constants (K) of the host to the guest was realized by UV–Vis spectroscopy titration experiments. The K values were calculated by applying

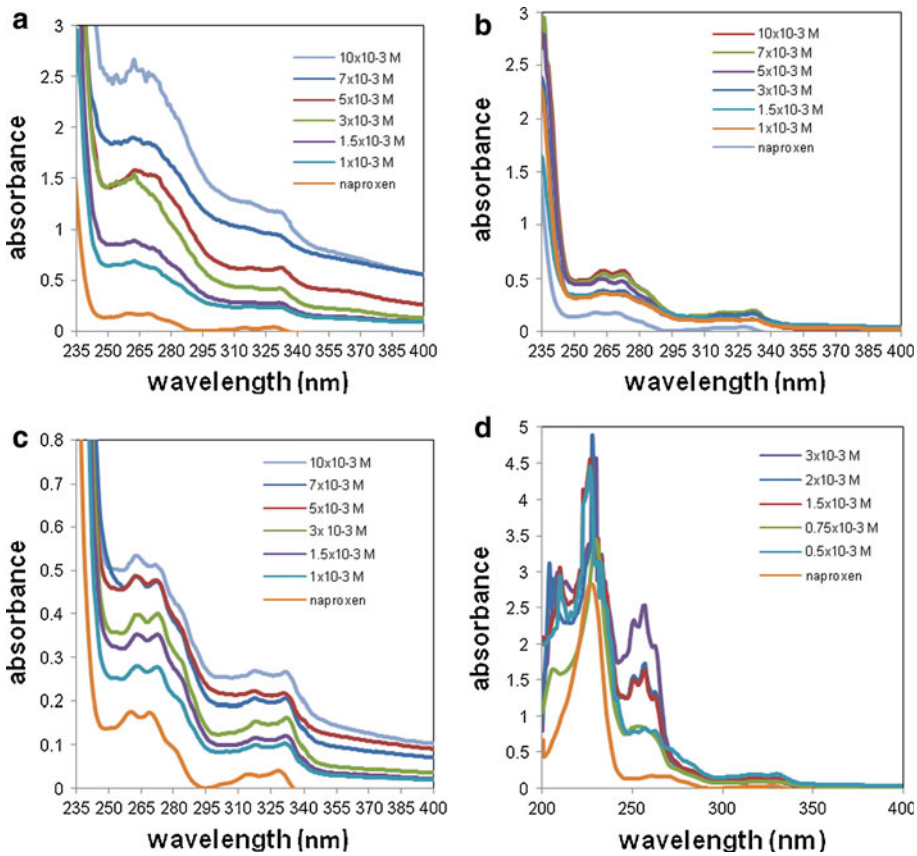

Fig. 3 UV absorption spectra of naproxen (2×10^{-3} M) in presence of **a** β-CD, **b** HP-β-CD, **c** β-CD-Hyd and **d** S-β-CD. The concentration of the hosts are in the range 0.0 to 12×10^{-3} M

least-squares fit to the plots of ([host]·[guest])/Δ*A* versus ([host] + [guest]), according to the modified Benesi-Hildebrand equation 2 [40, 41]:

$$\frac{[\text{host}][\text{guest}]}{\Delta A} = \frac{1}{K\Delta \in} + \frac{1}{\Delta \in}([\text{host}] + [\text{guest}]) \quad (2)$$

where, [guest] and [host] are the equilibrium concentrations of guest and hosts, respectively. Δε is the difference between the extinction coefficients of free and complexed guest. Δ*A* is the difference between the absorbances of free and complexed guest at the same wavelength.

Figure 4 shows the plots of ([host]·[guest])/ΔA versus ([host] + [guest]). The initial concentration of naproxen was kept at 2.0×10^{-3} M, while the concentrations of the hosts were in the range from 1 to 12×10^{-3} M. A linear least-squares fits to the plots. The *K* values of inclusion complexes of hosts with guest were determined from the slopes and intercepts of the linear plots based on the Eq. 2. The calculated *K* values of the inclusion complexes are summarized in Table 1. For all the four inclusion systems, the dependencies were linear in the investigated concentration range, confirming that the stoichiometries of the inclusion complexes in solution were 1:1 [42, 43].

For *β*-CD and derivatives, the changes in *K* values reflected the following order: S-*β*-CD > HP-*β*-CD > *β*-CD > *β*-CD-Hyd. The lowest K value for *β*-CD-Hyd system is attributable to the presence of water molecules inside its cavity hindering the entrance of the guest molecule. The greater complexing ability of HP-*β*-CD compared to *β*-CD might be due the restricted motion of the hydroxyl group on the HP-*β*-CD propyl moiety than the rim hydroxyls in *β*-CD [44]. One important use of HP-*β*-CD is to include insoluble drugs forming water soluble complexes so that stable water solutions can be prepared without organic solvents furthermore [45].

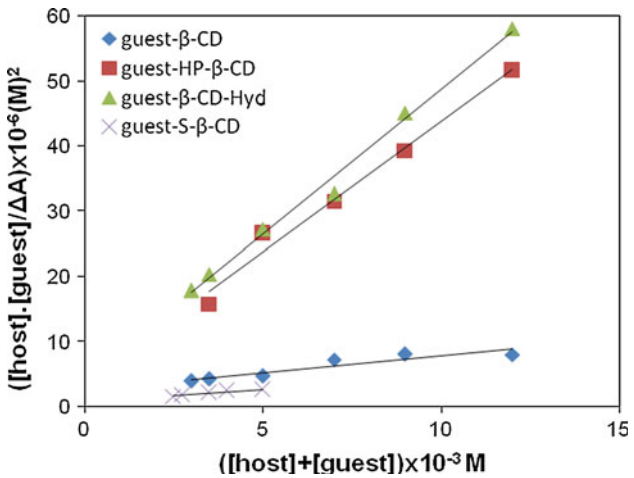

Fig. 4 Plot of ([host]·[guest])/ΔA versus [host] + [guest]

Table 1 Calculated *K* values of the complexes

Complex	*K* in (M)	Correlation coefficient
Naproxen-*β*-CD	1.9845	0.9299
Naproxen-HP-*β*-CD	3.5968	0.9888
Naproxen-*β*-CD-Hyd	1.0349	0.9961
Naproxen-S-*β*-CD	4.3023	0.9745

FTIR spectroscopic study

The FTIR spectrum of naproxen showed a sharp band at 1728 cm^{-1} and a broad band at 3302 cm^{-1} for carboxylic acid, which represented C=O and O–H stretching vibrations, respectively. This is in agreement with literature [46, 47]. All the four complexes we prepared through Freeze drying with *β*-CD and its derivatives showed that C=O band had changed in intensity and shifted its position significantly suggesting complex inclusion of that part of the molecule. The decrease in intensity of the C=O band may have resulted from its restriction within the *β*-CD cavity. For example, 80% reduction in intensity of the same band in case of naproxen was reported when complexed with *β*-CD [48]. The shifts of the O–H absorbance bands to higher frequency regions in all the complexes indicated the cleavage of the hydrogen bonding, further confirming the possibility of inclusion phenomena [38].

NMR spectroscopic study

Direct evidence for the formation of inclusion complex can be obtained from ^{1}H NMR [49]. ^{1}H NMR spectra of naproxen and the inclusion complexes of naproxen with *β*-CD, HP-*β*-CD, *β*-CD-Hyd and S-*β*-CD were recorded in $CDCl_3$ and D_2O, respectively. The values of chemical shifts, *δ* for different protons in naproxen and the naproxen-host complexes are listed in Table 2. The changes of chemical shift (Δ*δ*), for different protons in naproxen and complexes suggested complex formation. H1, H2 proton signals of naproxen were shifted up field in all the four complexes studied while the aromatic protons were shifted downfield. H3 protons were shifted up field in case of complexes with HP-*β*-CD, *β*-CD-Hyd and downfield for *β*-CD and S-*β*-CD.

In the NMR spectra of all the four complexes, magnitude of peak was lowered compared to the magnitude of peak for naproxen, which also indicated that there were changes in environment of hydrogen of naproxen molecule. This suggested formation of complex between guest and hosts, and this interaction may be due to intermolecular hydrogen bonding between guest and hosts [50].

Table 2 Chemical shift δ and $\Delta\delta$ of protons of naproxen in free guest and inclusion complex

	H1	H2	H3	Ar–H
Naproxen	1.5845	3.884	3.906	7.099–7.703
Naproxen + β-CD	1.483	3.809	3.930	7.212–7.810
$\Delta\delta$	−0.1015	−0.075	0.024	0.113–0.107
Comment	Up field	Up field	Down field	Down field
Naproxen + HP-β-CD	1.441	3.647	3.905	7.196–7.832
	−0.1435	−0.237	−0.001	0.097–0.129
Comment	Up field	Up field	Up field	Down field
Naproxen + β-CD-Hyd	1.459	3.693	3.891	7.157–7.773
	−0.1255	−0.191	−0.015	0.058–0.07
Comment	Up field	Up field	Up field	Down field
Naproxen + S-β-CD	1.492	3.789	3.953	7.218–7.870
	−0.0925	−0.095	0.047	0.119–0.167
Comment	Up field	Up field	Down field	Down field

The hydrogen atoms are labelled in Fig. 1b

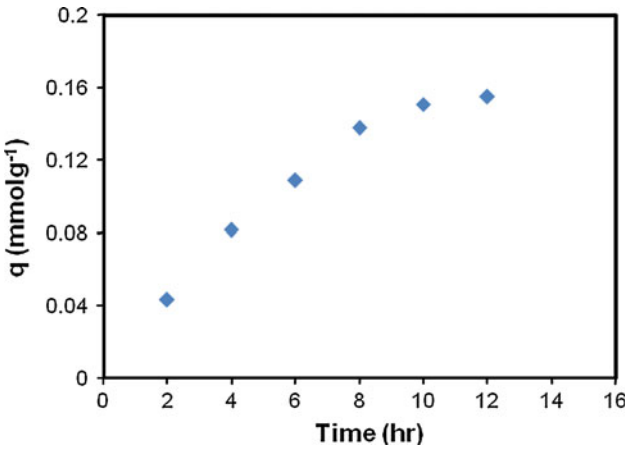

Fig. 5 Adsorption rate curve for naproxen on CDS

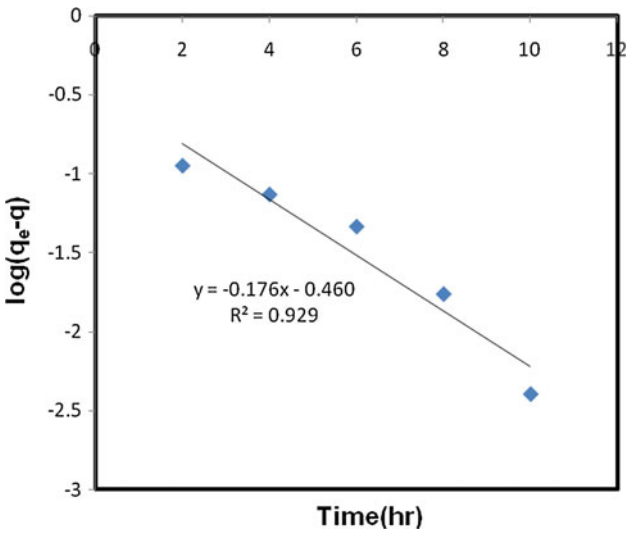

Fig. 6 Pseudo first order plot for adsorption of naproxen on CDS

Adsorption of naproxen onto CDS

Naproxen (a derivative of 2-arylpropionic acid) was used as an adsorbate in this work. Prior to obtaining the isotherm for adsorption process, a kinetic study will be useful to ascertain the minimum length of time necessary to reach equilibrium. Adsorption rate curve for naproxen on CDS were generated at a stirring speed of 800 rpm as shown in Fig. 5. Adsorption kinetics was examined with Lagergren's first order and Ho's second order kinetic equations [51]. Both equations are based on the adsorption of an adsorbate from a solution onto solid adsorbents and are usually referred to as pseudo-first and pseudo-second order kinetic models, respectively [52].

The pseudo-first order or Lagergren equation is:

$$\log(q_e - q) = \log q_e - \left(\frac{K_1}{2.303}\right)t \qquad (3)$$

where q_e and q are the amounts of naproxen adsorbed (mmol g^{-1}) at equilibrium and time (t), respectively and K_1 (S^{-1}) is the pseudo-first order rate constant or adsorption rate constant. Figure 6 shows the plots of log ($q_e - q$) vs. t, indicating that first order kinetics provided a good representation of the experimental data with $R^2 \geq 0.929$ for naproxen.

The linearised form of the pseudo-second order equation is provided below [53]:

$$\frac{t}{q_t} = \frac{1}{K_2 q_e^2} + \left(\frac{1}{q_e}\right)t \qquad (4)$$

The values of q_e and K_2 can be estimated from the slope and the intercept of the plot (t/q_t) versus t. The product $K_2 q_e^2$ represents the initial adsorption rate. Figure 7 showing the plots of (t/q_t) vs. t, indicates that pseudo-second order equation with $R^2 \geq 0.948$ for naproxen provide a better representation of the experimental data compared to the first order equation. It was shown that the pseudo second-

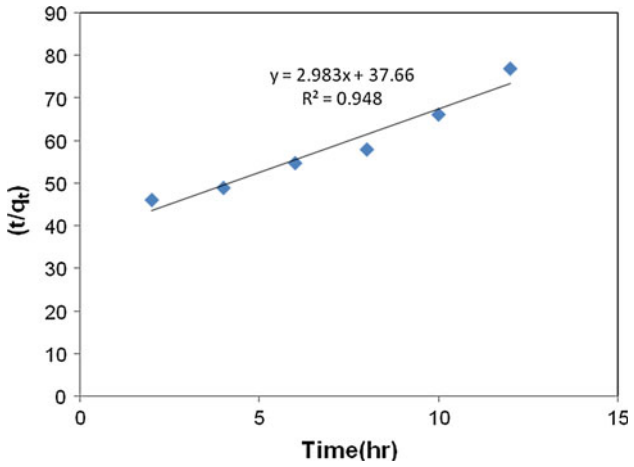

Fig. 7 Pseudo second order plot for adsorption of naproxen on CDS

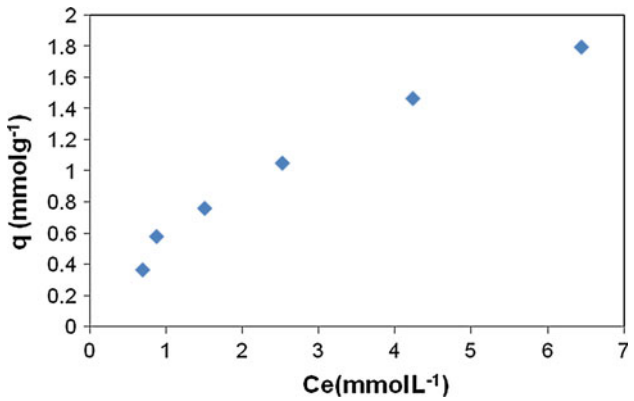

Fig. 8 Adsorption isotherm of naproxenon CDS at pH 8

order kinetic equation could describe the adsorption kinetics for naproxen sodium onto activated carbon [54].

Figure 8 shows the adsorption isotherm of naproxen on CDS. The increase in the adsorption affinity with increasing amounts of CDS, corresponded to increasing interactions between adsorbate and CDS. This showed that the inclusion phenomena played a major role in the adsorption mechanism. The Langmuir and Freudlich isotherms are the most frequently used equations to plot data corresponding to adsorption from solution measurements [55]. Freundlich isotherm was used to describe equilibrium adsorption data, because different energy adsorption sites are expected in the polymeric network [56]. The fitting parameters for the Freundlich isotherm ($q_e = K_f C_e^n$) are $K_f = 5.9340$, $n = 6.0544$ and with $R^2 \geq 0.996$.

Characterisation of unloaded and naproxen/CDS loaded adsorbent

Figure 9a shows the micrograph of a β-CD bonded silica stationary phase (CDS) used as an adsorbent. The scanning electron micrograph of CDS appeared as aggregates of irregularly shaped crystals [38] and possessed a porous structure, which should significantly increase the available surface area of the CDS and, therefore, increase the adsorption capacity. The SEM of naproxen appeared as of distorted tubular shapes and sizes and, tended to form aggregates (Fig. 9b). The morphology of CDS after adsorption (Fig. 9c) showed large plate like crystals where guest molecules are embedded losing its original distorted tubular shaped like structures demonstrating inclusion phenomena.

FTIR spectrum of CDS showed peak at 3448.09 cm^{-1}, which can be assigned to the presence of OH group. The absorption peak at 1654.58 cm^{-1} was possibly caused by the presence of the hydroxyl groups participating in an aromatic system. The changes in band positions to 3460 cm^{-1} and 1645 cm^{-1} in the IR spectrum of naproxen after adsorption on CDS were attributable to the formation of hydrogen bonds with CDS.

Optimized binding energy

Naproxen (Fig. 1b) possesses a propanoate group and a methoxy group linked to a naphthalene ring. In naproxen-β-CD system the propanoate moiety of naproxen preferred to form hydrogen bonds with the primary hydroxyl group of β-CD rather than the secondary hydroxyls [57]. Van der Waals interaction was found between the ring hydrogen of β-CD and the hydrogen of the naphthalene ring. Moreover, the side view of the complex in Fig. 10a displayed that more than half of the naphthalene ring of the naproxen molecule was included into the inner hydrophobic cavity of torus shaped β-CD while the methoxy group on the naphthalene ring exposes itself towards the solution.

Naproxen-HP-β-CD (Fig. 10b) showed same type of interaction as naproxen-β-CD system and the inclusion of naphthalene ring was almost similar but here the methoxy group had Van der Waal interaction with the hydroxypropyl group of host which gave a restriction to the flexibility of the naproxen molecule or of the host making the complex more rigid.

In S-β-CD complex with naproxen (Fig. 10c), the interaction was almost similar as mentioned above for the other two systems. However, in this case the methoxy group was directed towards the solution forming intermolecular hydrogen bond and also showed Van der Waals interaction with the sulphated sodium portion of the S-β-CD. Again the naphthalene ring remained fully included into the inner cavity which was an added advantage over the two systems as inclusion was most dominant here.

Energy changes involved in host–guest inclusion processes obtained by applying semiempirical PM3 calculations are given in Table 3. As shown in Table 3, the negative values of ΔE ranging from -96.6184 to -26.5175 kJ mol^{-1} clearly revealed that the formations of

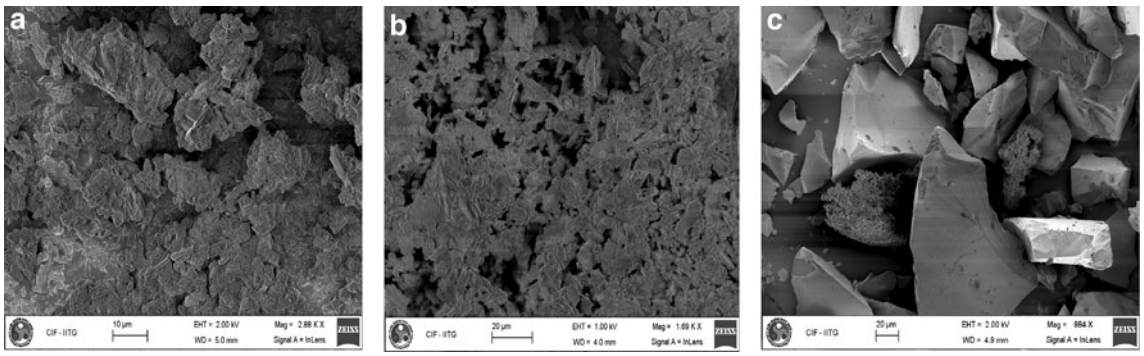

Fig. 9 Scanning electron micrographs for **a** CDS, **b** naproxen and **c** naproxen after adsorption on CDS

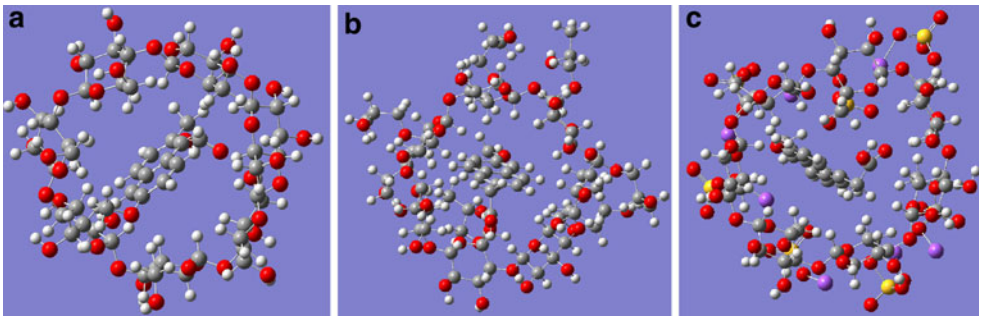

Fig. 10 Optimized structures computed for complexes of naproxen with **a** β-CD, **b** HP-β-CD, and **c** S-β-CD

Table 3 Calculated ΔE values of host–guest complexes

Complex	ΔE in KJ mol^{-1}
Naproxen-β-CD	−26.5175
Naproxen-HP-β-CD	−48.8343
Naproxen-S-β-CD	−96.6184

the inclusion complexes are all energetically favourable. The bigger absolute values of the binding energies lead to the higher stabilities of the complexes. The binding energy values obtained from the PM3 calculation showed the same relation with the formation constant values determined by UV–Vis spectroscopy. Thus, the processes involving naproxen and S-β-CD is preferential. The higher stabilization energy of HP-β-CD compared to β-CD is an added advantage as HP-β-CD have attracted growing interest due their improved complexing ability, greater water solubility and less toxicity [16]. These results indicated that the best complexation of the naproxen occur with S-β-CD, suggesting that this is a choice in oral formulations for the treatment of osteoarthritis, rheumatoid arthritis and acute pain in musculoskeletal disorders.

Conclusion

This investigation constituted a physicochemical characterization of the interaction of β-CD, three of its chemically modified variety, its polymer bonded to silica gel with nonsterodial anti-inflammatory drug, naproxen. Spectroscopic and morphological studies have been done in order to study the possibility of interactions between the guest and the β-CD molecules. CDs as drug carrier increase the solubility, bioavailability and stability of poorly water soluble drugs. CDs were also reported to reduce drugs irritations, reduce or prevent gastrointestinal irritation and thus the prepared complexes are expected to reduce the untoward side effects associated with drugs and to enhance the oral bioavailability of it. Molecular modeling studies corroborate the experimental data showing that the results are consistent. UV–Vis, NMR and FTIR spectroscopy results demonstrated the inclusion. In the inclusion process intermolecular hydrogen bonding and Van der Waals interactions were found to be the most prominent interactions. From comparative assessment of inclusion properties, we got that among the systems studied two chemically modified varieties (i.e. HP-β-CD and S-β-CD) were more preferable for inclusion compared to native β-CD and of which S-β-CD system was the most, which might possibly give further hopeful applications like chiral separations etc. The β-CD polymer functionalized on silica gel also represented a very interesting choice for inclusion with the guest molecule.

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