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Calorimetric study of the interactions between surfactants and dextran modified with deoxycholic acid

Guangyue Bai · Vasco Castro · Marieta Nichifor · Margarida Bastos

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Abstract Dextran modified with deoxycholic acid (Dex-DCA) was synthesized by grafting DCA along the polymer backbone, with degrees of substitution (DS)—2% and 3%. The thermodynamics of the association processes of the mixed systems is followed by isothermal titration calorimetry for sodium deoxycholate/sodium dodecyl sulfate (NaDCA/NaDS), Dex-DCA with different surfactants—Dex-DCA/NaDS, Dex-DCA/NaDCA, and Dex-DCA/DTAB (dodecyltrimethylammonium bromide). Calorimetric measurements for the micellization processes of the pure surfactants in aqueous solution were also performed for comparison with the results obtained for the mixed systems. We have obtained and herein present the enthalpies of micelle formation and critical micelle concentrations for the referred pure surfactants, as well as the interaction and aggregation enthalpies for the mixed systems-surfactant/polymer. The dependence of the observed aggregation behavior on the surfactant and temperature is discussed in detail. Finally, we should stress that calorimetry allowed us to ascertain a very important fact in polymer/surfactant interaction. From the comparison between NaDCA/NaDS and Dex-DCA/NaDS calorimetric titration curves, we could clearly see that the interaction between Dex-DCA and NaDS is driven by the interaction between the bile acid moiety and the surfactant.

G. Bai · V. Castro · M. Bastos (✉)
CIQ (UP), Department of Chemistry, Faculty of Sciences, University of Porto, R. Campo Alegre, 687, 4169-007 Porto, Portugal
e-mail: mbastos@fc.up.pt

M. Nichifor
"Petru Poni" Institute of Macromolecular Chemistry, 700487 Iasi, Romania

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Introduction

Bile salts (BS) are a very important class of biosurfactants. They can form a variety of aggregates and micelle structures in aqueous solution [1–4]. BS micelles are capable of incorporating different lipids and detergents to form mixed micelles, which exhibit a great potential in life science and in biomedical applications [5–9].

Bile acids can also be grafted to the hydrophiphilic backbone of polymers as side chains, providing very interesting amphiphilic polymers [10–18]. These polymers should present a self-aggregation behavior similar to surfactants (main differences arising from conformational constraints), with the advantage of a better compatibility with biological systems.

In previous work, the synthesis of a series of hydrophobically modified dextrans (Dex-DCA and Dex-CA) was reported [10] and their interesting aggregation properties were addressed by different fluorescence and light scattering techniques [11]. It was shown that these modified polymers can indeed self-assemble to form aggregates of different size depending on concentration range and bile acid type.

In aqueous media, BS aggregation properties are very different from those of common ionic surfactants [3–5], because of their characteristic structural features—they are composed of a rigid steroid skeleton with a hydrophilic and a hydrophobic surface, instead of the typical

"head-and-tail" structure of conventional surfactants [19–22]. Indeed this also leads to different aggregation behavior for polymers grafted with bile acids or with conventional alkyl chains. Therefore, it is of particular importance to understand and compare these differences in aggregation behavior resulting from the structural differences in the substituents or pendent groups in the polymer.

In recent years, some studies were published on systems of BS and other surfactants [21–24] or with polymers [25–27]. However, reports concerning the thermodynamics of their interaction are relatively scarce. It is clear that more detailed thermodynamic information about interactions in these mixed systems can provide a quantification of their energetics as well as a better understanding of their interaction mechanism. Microcalorimetry presents distinct advantages for this purpose by characterizing simultaneously the critical concentrations and the energetics of various interactions, and identifying factors and driving forces that govern the interactions in such systems. In fact, calorimetry has proven to be the most sensitive technique for directly measuring the thermodynamic properties of aggregation in this type of systems [28–36]. Therefore, a microcalorimetric study of the mixed systems containing BS or bile acid modified dextran will characterize in detail the thermodynamic behavior of these mixed systems.

In the present work, we studied the interaction of sodium deoxycholate (NaDCA) with a surfactant of the same charge, sodium dodecyl sulfate (NaDS), with the aim to characterize and ascertain the role of the hydrophobic effect on the association. Modified dextrans were synthesized by Nichifor et al. [10] by covalent attachment of deoxycholic acid (DCA) to the dextran backbone through ester links (Dex-DCA). It is known that the association between hydrophobically modified polymer (HMP) and surfactants is similar to the surfactants' mixed micellization [37]. It is thus to be expected that the interactions between the polymers studied here, Dex-DCA (DS 2 and 3%) and NaDS or NaDCA, share some characteristics with the interactions observed between the two anionic surfactants.

The thermodynamic characterization of the interactions was obtained from isothermal titration calorimetry (ITC) measurements. To discriminate the importance of the various components of the interaction, we did follow calorimetrically (i) the dilution of the studied surfactants (NaDCA, NaDS and DTAB) into water; (ii) the interaction between surfactants of the same charge (NaDS and NaDCA); and (iii) the interaction of Dex-DCA with surfactants (NaDS or NaDCA and DTAB). The thermodynamic information obtained from (i) and (ii) is used to provide further understanding of the energetics of the HMP (Dex-DCA) and surfactants systems.

Experimental

Materials

NaDCA (Merck, 99%), NaDS (Sigma, 99%), and dodecyltrimethylammonium bromide (DTAB) (Fluka, 99%) were used without further purification.

The studied polymer, deoxycholic acid modified dextran (Dex-DCA) with degrees of substitution (DS) of 2% and 3% was synthesized according to previously described methods [10]. Briefly, the polymer (Fig. 1) was obtained by reacting dextran (M_w = 30,200, M_w/M_n = 1.112) with deoxycholic acid in the presence of *N*,*N*-dicyclohexylcarbodiimide as a coupling agent and 4-(*N*,*N*-dimethylamino) pyridine as a catalyst.

All solutions were prepared by volume, using water produced by a Milli-Q filtration system. Surfactant concentration is reported in mol dm^{-3} and polymer concentration in g dL^{-1}.

Isothermal titration calorimetry

The microcalorimetric unit used in this work, as well as the experimental procedure, have been described in detail in our previous work [34]. Briefly, the calorimetric titration experiments consisted of a series of consecutive additions of concentrated surfactant solution into water, NaDCA, and polymer solution. The volume of the solution in the calorimetric vessel was 2.6 cm^3 (polymer solution, NaDCA

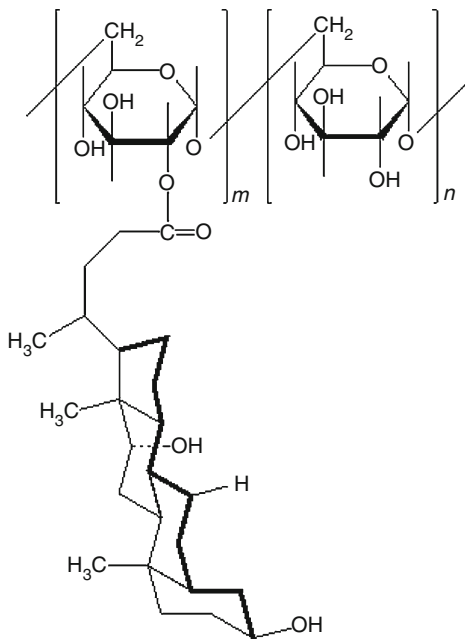

Fig. 1 Chemical structure of the studied polymers (Dex-DCA) obtained by hydrophobic modification of dextran

solution, or water) The titrating solution was added to the calorimetric vessel in aliquots of 4–8 μL, from a modified gas-tight Hamilton syringe, through a thin stainless-steel capillary, until the desired range of concentration had been covered. The injections were computer controlled. A Kel-F turbine, made for us at the workshop of Lund University (Sweden) was used throughout, as it proved to promote very good mixing [34]. All experiments were performed at 308.15 and 298.15 (±0.01 K).

Results and discussion

Micellization of the surfactants in aqueous solution

ITC measurements were performed on two anionic surfactants (NaDCA and NaDS) and one cationic surfactant (DTAB) at two different temperatures ($T = 298.15$ and 308.15 K). NaDS and DTAB have the typical structure of conventional surfactants "polar head-and-apolar hydrocarbon tail". Although thermodynamic data are already available for these two surfactants at the studied temperatures, we did measure their dilution into water in the conditions used in the polymer/surfactant experiments for the purpose of comparison with the mixed systems involving the polymer or NaDCA (see the later text).

In aqueous media, BS are described in terms of a lipophilic surface, which is the convex side of the rigid steroid ring system, and a hydrophilic surface, which is the polyhydroxylated concave side of the molecule [19, 20]. Therefore, their micellization behavior is expected to be different from conventional ionic surfactants having a lipophilic part as a flexible aliphatic chain. The calorimetric curves obtained for the change of the observed enthalpies of dilution (ΔH_{obs}) against surfactant concentration (C) are shown in Fig. 2(a–c) for the three surfactants. The dilution process was endothermic, and hence the enthalpies of micelle formation for these surfactants are negative, at the two studied temperatures.

In the conditions used, NaDCA, NaDS, and DTAB were well above their critical micelle concentrations (cmcs) in the initial concentrated solutions in the syringe. In general, the initial addition of concentrated surfactant solution produces a diluted solution in the sub-micellar region. Two processes occur: (1) the micelles that have been added dissociate into monomers and (2) then the monomer solution is further diluted. When the final concentration is above the cmc, the only effect is the dilution of the added micelles. It is worth noting that the concentration range corresponding to the micellization process of the BS NaDCA is obviously broader than the one observed for the aliphatic surfactants NaDS and DTAB. The width of the concentration range over which micellization occurs

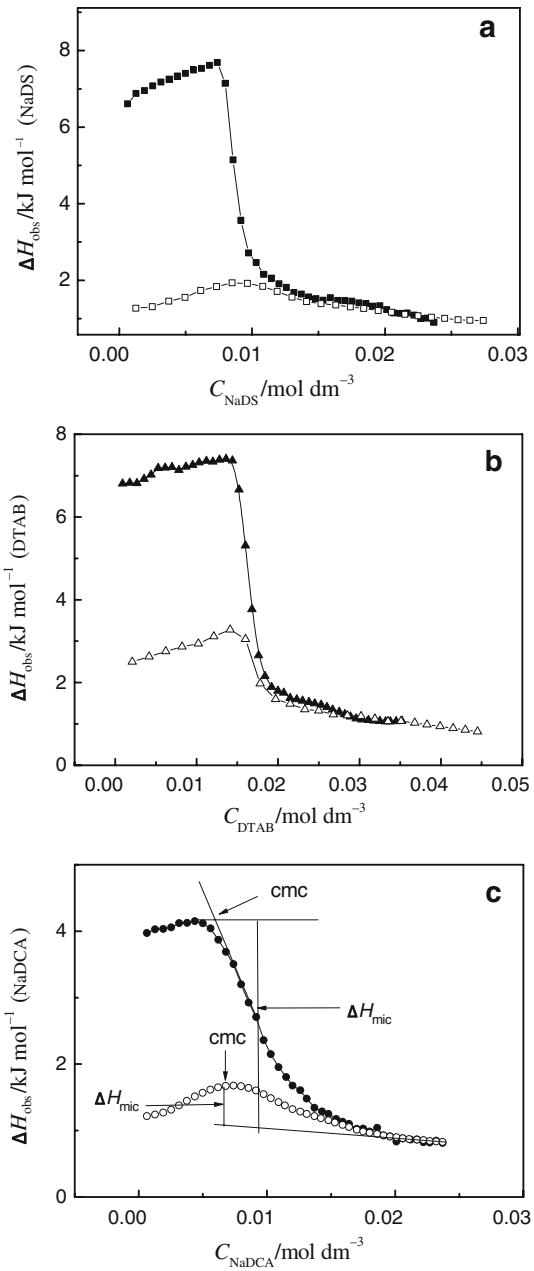

Fig. 2 Microcalorimetric titration curves for dilution of NaDS (0.2 mol dm^{-3}), DTAB (0.28 mol dm^{-3}), and NaDCA (0.2 mol dm^{-3}) into water at 308.15 K (*full symbols*) and at 298.15 K (*empty symbols*)

reflects the cooperativity of the micellization process. In the case of deoxycholate, the larger concentration range observed for micellization implies that the micelle aggregate is changing as the NaDCA concentration increases, probably due to a change in aggregation number. It was found that pure NaDCA micelles have much smaller aggregation numbers and that the micellization process follows a stepwise incorporation of monomers over a broader concentration range [38–40]. Further we observed

that the curve for the dilution of NaDCA at $T = 298.15$ K seems to be similar to those of aliphatic surfactants having a shorter alkyl chain and a smaller aggregation number [41, 42]. Before cmc, ΔH_{obs} increases with the concentration of NaDCA, in agreement with the usual dilution pattern. After cmc, the ΔH_{obs} decreases gradually until about three times cmc. This suggests a large deviation from the phase separation model [43]. In order to have a common basis for comparison of the thermodynamic parameters for the three surfactants and their interactions with the polymer, we did determine their cmc's and the enthalpies of micellization, ΔH_{mic} from the calorimetric curves according to usual methods and principles [44, 45], also described by us before [41, 42] (Fig. 2c). From the variation of ΔH_{mic} with temperature the values for the change in heat capacity over the studied temperature range ($\Delta C_{p,mic}$) were derived. All the thermodynamic parameters for the micellization of the three surfactants at the studied temperatures, $T = 298.15$ and 308.15 K, are summarized in Table 1.

The cmc's and ΔH_{mic} values for the conventional surfactants NaDS and DTAB are in good agreement with reported values in the literature [46–48]. For NaDCA, we did not observe from our calorimetric tracings the two cmc's that were reported by Ninomiya et al. [39] and Matsuoka et al. [40] that were obtained by fluorescence. The value we obtain for cmc is in good agreement with the one suggested for the second cmc in the reference above [39, 40]. The ΔH_{mic} values of NaDCA at 298.15 K are in good agreement with those obtained from calorimetric method by Paula et al. [19]—cmc = 5.5 mmol dm^{-3} and $\Delta H_{mic} = -0.6$ kJ mol^{-1} at 298 K. Although they do not report a value for $T = 308.15$ K, we did calculate from their data, obtaining –3.0 kJ mol^{-1}, in agreement with our value for the same temperature.

Increasing the temperature leads to an increase in the negative enthalpy of micellization, leading to a negative $\Delta C_{p,mic}$. This is a common feature of amphiphiles association in aqueous solution, as the major driving force for micelle formation is the hydrophobic effect. This effect also drives a gain in entropy (ΔS) due to hydration water around the hydrophobic parts of the monomeric amphiphiles being released to bulk water during the micellization process. $\Delta C_{p,mic}$ has been reported to be a linear function of the hydrophobic surface area of the amphiphile that gets excluded from water through the micellization process [49]. Thus, the $\Delta C_{p,demic}$ ($=-\Delta C_{p,mic}$) can provide an indication of whether more hydrophobic surface is exposed to water when the aggregates dissociate into monomers. The change in $\Delta C_{p,mic}$ is calculated as

$$\Delta C_{p,mic} = [\Delta H_{mic}(308.15\,K) - \Delta H_{mic}(298.15\,K)]/\Delta T$$

assuming a linear dependence of ΔH_{mic} on temperature in this small temperature interval. The obtained values in the present work are in agreement with reported values within our calculated error (about ± 100 J K^{-1} mol^{-1}). For DTAB, we obtained -352 J K^{-1} mol^{-1} and the $\Delta C_{p,mic}$ was reported to be -346 J K^{-1} mol^{-1} [48] and -406 J K^{-1} mol^{-1} [47]. For NaDS we obtained -500 J K^{-1} mol^{-1} and Paula et al. [19] report $\Delta C_{p,\,mic} = -450$ J K^{-1} mol^{-1} ($T = 298$ K) and from the ΔH_{mic} obtained by Wang and Olofsson [46] we calculated a $\Delta C_{p,mic}$ of -510 J K^{-1} mol^{-1}. For NaDCA, we obtained -245 J K^{-1} mol^{-1} and the literature value obtained by calorimetry was $\Delta C_{p,mic} = -360$ J K^{-1} mol^{-1} ($T = 298$ K) [19, 20]. The value for $\Delta C_{p,mic}$ of NaDCA is smaller than the ones obtained for the other two surfactants. This indeed reflects the different molecular structure of NaDCA as compared to NaDS and DTAB, leading to a smaller fraction of the hydrophobic surface removed from water upon micellization, and thus to a significantly lower $\Delta C_{p,mic}$.

Interaction between NaDCA with NaDS—same charge surfactants

Mixture of two surfactants usually form mixed micelles at very low concentration. In this study, we have a mixture between a classical "head–tail" aliphatic surfactant and a special type of surfactant, BS, which makes it of great interest [22]. The interaction of NaDS with NaDCA was followed by ITC and compared to the micellization behavior of the pure NaDS in aqueous solution. In parallel with this aim, we also wanted these results to be compared with the calorimetric tracings of the titration of Dex-DCA with NaDS.

From the observed heat in each injection of NaDS (syringe) into NaDCA solution (in the vessel), the observed

Table 1 Enthalpies of micellization (ΔH_{mic}) and critical micelle concentrations (cmc) for the studied surfactants at 298.15 K and 308.15 K

Surfactants	Cmc[a]/mmol dm^{-3}		ΔH^{b}_{mic}/kJ mol^{-1}		$\Delta C^{b}_{p,mic}$/J K^{-1} mol^{-1}
	298.15 K	308.15 K	298.15 K	308.15 K	
NaDS	7.9	8.1	−0.35	−5.35	−500
NaDCA	6.3	6.0	−0.50	−2.95	−245
DTAB	15.2	14.9	−1.82	−5.34	−352

[a,b] The estimated error for surfactants' cmc and ΔH_{mic} is <4%

enthalpies were calculated. The obtained values for ΔH_{obs} as a function of NaDS concentration, C_{NaDS}, for different initial NaDCA concentrations in the vessel are plotted in Fig. 3 for $T = 308.15$ K. The results exhibit a very different profile when C_{NaDCA} (in the vessel) = 2.4 mmol dm^{-3} ($C_{NaDCA} <$ cmc) or when C_{NaDCA} (in the vessel) = 12.1 and 24.1 mmol dm^{-3} ($C_{NaDCA} >$ cmc) (cmc(NaDCA) = 6.0 mmol dm^{-3}, see Table 1). For the curve where $C_{NaDCA} = 2.4$ mmol dm^{-3} we observe a clear break, and the onset of the break is at a concentration of NaDS of 2.1 mmol dm^{-3} smaller than the cmc of pure NaDS. This means that we are in fact observing the onset of mixed micelle formation. Thus, the cmc of the 1:1 mixture of NaDS + NaDCA is the total surfactant concentration at this point, i.e., $cmc_{mix} = 4.5$ mmol dm^{-3}. This result is consistent with the one obtained by Jana and Moulik [21]. The cmc_{mix} is smaller than both NaDS and NaDCA, suggesting a synergistic effect between the two surfactants.

When NaDCA concentration in the vessel is above its own cmc (Fig. 3), the continuing addition of NaDS monomers induces the formation of mixed micelles, owing to NaDS monomer insertion in already formed NaDCA micelles. Further, as we observe a decrease in ΔH_{obs} (in absolute values) followed by a leveling off, we believe that an increase in the aggregation number of the NaDS/NaDCA mixed micelles occurs with NaDS addition, meaning that structural rearrangements did occur in the mixed micelles upon increasing NaDS concentration.

From Figs. 3 and 4 (interactions at $T = 308.15$ and 298.15 K, respectively), we observe that in the initial concentration range ($C_{NaDS} <$ cmc) the addition of NaDS monomers to NaDCA micellar solution ($C_{NaDCA} = 12.1$ or 24.1 mmol dm^{-3}) induces a deviation of the ΔH_{obs} versus C_{NaDS} curves from the curve representing NaDS dilution into water. Hence the enthalpies of interaction (ΔH_{int}) of

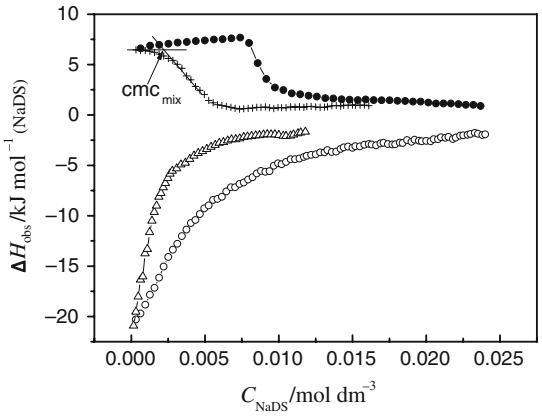

Fig. 3 Variation of the observed enthalpies with NaDS concentration for NaDCA/NaDS systems at $T = 308.15$ K. NaDCA concentrations in the calorimetric cell are 2.4 mmol dm^{-3} (+), 12.1 mmol dm^{-3} (Δ), and 24.1 mol mdm^{-3} (○). Curve (●) is for the dilution of the concentrated NaDS solution (0.2 mol dm^{-3}) into water

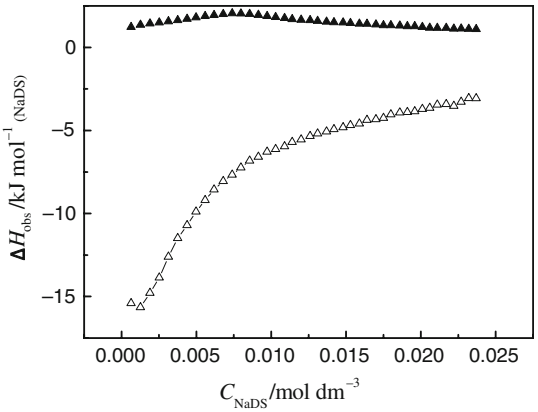

Fig. 4 Variation of the observed enthalpies with NaDS concentration for NaDCA/NaDS systems at $T = 298.15$ K. The NaDCA concentration in the calorimetric cell is 1.0 g dL^{-1} (Δ). Curve (▲) is for the dilution of the concentrated NaDS solution (0.2 mol dm^{-3}) into water

NaDS with NaDCA can be roughly estimated from the difference between the observed enthalpies on the two curves [50]. The calculated values obtained for the first injection at $C_{NaDCA} = 24.1$ mmol dm^{-3} were $\Delta H_{int} \approx -27.8$ kJ mol^{-1} at $T = 308.15$ K and $\Delta H_{int} \approx -16.9$ kJ mol^{-1} at $T = 298.15$ K. These ΔH_{int} values reflect the extent of interaction between the two surfactants. As mentioned above, NaDCA does not possess a polar-head group and an apolar hydrocarbon tail. Instead, it is better described in terms of having a hydrophobic and a hydrophilic molecular surface. Formation of NaDS-NaDCA mixed micelles leads to larger exothermic values in the initial stages of NaDS addition. The insertion of NaDS is mainly caused by the favorable hydrophobic interaction between the alkyl chain of NaDS monomers and the hydrophobic surface of NaDCA. We observe a leveling-off at all curves, meaning probably the occurrence of saturation of NaDCA micelles with NaDS monomers, and the curves tend to the dilution of pure NaDS. Finally, we should refer that from the values above we see that ΔH_{int} depends on temperature, giving rise to a negative $\Delta C_{p,int}$.

Interactions between surfactants and hydrophobically modified dextran (Dex-DCA)

Both the association's mechanism and the strength of the interactions depend to a large extent on a number of factors, such as the molecular architecture of the polymer, the surfactant's type, the concentration of the polymer and surfactant and the ratio between surfactant and pendant hydrophobic groups, the hydrophobicity/hydrophilicity of the polymer backbone, the hydrophobicity of pendant groups, etc. A detailed thermodynamic study and derived parameters can give valuable insight into the nature and strength of the interactions.

Calorimetric titration measurements were performed for the following surfactant/polymer systems—Dex-DCA/NaDS or Dex-DCA/NaDCA and Dex-DCA/DTAB, at 308.15 and 298.15 K, at different polymer concentrations ($C_p = 0.1–1.0$ g dL^{-1}). In the studied polymer concentration range, dextran modified with DCA forms micellelike aggregates with critical aggregation concentrations $\leq$0.1 g dL^{-1} (for DS between 2% and 5% [11]) much lower than the cmc of NaDCA. To properly compare with our cmc value for the surfactant NaDCA, we did calculate the polymer cac as expressed in the concentration of the pendant groups (DCA). For Dex-DCA (DS = 2%), the value reported was—cmc (in polymer concentration) $\approx$ 0.10 g dL^{-1}, whereas the value we now calculate from it is cac (concentration of pendent group) = 0.12 mmol/dm^3.

At lower polymer concentration ($C_p < 0.02$ g dL^{-1}), the modified polymer forms big and loose aggregates, and with increasing polymer concentration small and compact ones start to form [11]. The effect of polymer concentration on the interactions with surfactants can be seen from the variation of the observed enthalpies (ΔH_{obs}) with NaDS concentration (C_{NaDS}) when different polymer concentrations in the vessel are used (Fig. 5). All curves present a similar pattern, but as the polymer concentration decreases we can see two effects—the interaction is weaker, and the curve tends to pure surfactant dilution. The observed pattern shares common features with other systems of nonionic HMP and surfactants [51]. Analyzing now in detail, we can see that compared with the corresponding enthalpy of dilution curve for NaDS into water, the ΔH_{obs} versus C_{NaDS} curves for polymer/surfactant deviate in the beginning of the titration quite significantly in the exothermic direction. This effect is particularly strong when the polymer concentration is above 0.5 g dL^{-1}, giving rise to an exothermic ΔH_{obs}. It is known that when the polymer concentration is larger than >0.2 g dL^{-1} the aggregates are very small and very compact [11], and their behavior seems to be similar to our previously studied systems [50, 51]. All but one of our systems are in this concentration range. When SDS concentration is very low, the added SDS micelles dissociate first into monomers, and then the SDS monomers are dissolved in hydrophobic polymer aggregates, until the Dex-DCA aggregates start to disintegrate and the rehydration of polymer backbone occurs [33].

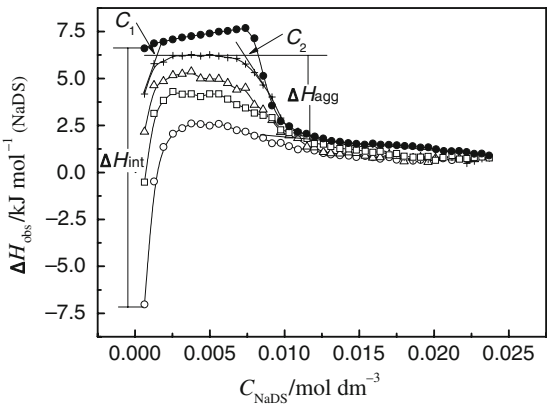

Fig. 5 Variation of the observed enthalpies with NaDS concentration for Dex-DCA(DS = 2%)/NaDS systems at $T = 308.15$ K. Titration of NaDS (0.2 mol dm^{-3}) into pure water (●). The concentrations of polymer solutions: 1.0 g dL^{-1} (○), 0.5 g dL^{-1} (□), 0.25 g dL^{-1} (Δ), and 0.1 g dL^{-1} (+), respectively

Although the increase in hydrophobic side group concentration (i.e., higher polymer concentrations) results in strengthening the intermolecular association between different polymer chains, the aggregates formed with this polymer have low aggregation numbers, because the pendant groups, i.e., the bile acid moiety, are characterized by a rigid ring structure and an hydrophobic and the hydrophilic surface. As a result, the addition of NaDS leads to the surfactant-induced break-up of polymer aggregates and consequent rehydration of polymer backbone and the hydrophilic surface of bile acid moiety. This reflects in the large exothermic enthalpy observed at low surfactant concentration.

The total observed enthalpy must be the net result of demicellization of the surfactant (endothermic contribution) and surfactant monomer/polymer interaction (exothermic contribution). Accordingly, we can calculate the enthalpy of interaction of polymer/surfactant, ΔH_{int}, by subtracting the dilution enthalpy of pure surfactant from total observed enthalpy, as shown in Fig. 5. The detailed thermodynamic description is provided in our previous work [50, 51]. The interaction enthalpies at the first injection were calculated for all studied systems, and the values are given in Table 2. We found that increasing the polymer concentration results in a linear increase in the exothermic interaction enthalpy.

When NaDS concentration reaches C_1 (see Fig. 5), mixed micelles start to form, involving the alkyl chain of the surfactant and the bile acid moiety of the polymer. At this point, the polymer is probably already re-hydrated and therefore the smaller exothermic interaction enthalpies reflect the hydrophobic interaction between the alkyl chains and hydrophobic surface of the rigid ring of bile acid. Between C_1 and C_2 the interaction enthalpies change only slightly with increasing NaDS concentration, but in this concentration range ΔH_{int} values depend on polymer concentration. When the polymer concentration increases, the relative number of bile acids involved in mixed micelle aggregates also increases, and therefore the number of surfactant monomers involved in mixed micelle aggregates also increases, the interaction enthalpy also increases, and

Table 2 Interaction enthalpies (ΔH_{int}) and enthalpies of aggregation (ΔH_{agg}) for Dex-DCA/surfactant systems

Systems	$C_{polymer}$/g dL^{-1}	$10^3 \times C^{a}_{side\ group}$/mol dm^{-3}	$\Delta H^{b,c}_{int}$/kJ mol^{-1}	ΔH^{c}_{agg}/kJ mol^{-1}	T/K
NaDS + Dex-DCA (DS = 2%)	0.1	0.12	−2.4	−4.5	308.15
	0.25	0.30	−4.5	−3.6	
	0.5	0.59	−7.1	−2.8	
	1.0	1.18	−13.6	−1.6	
DTAB + Dex-DCA (DS = 2%)	1.0	1.18	−2.0	−4.4	308.15
NaDS + Dex-DCA (DS = 3%)	1.0	1.73	−11.0	–	298.15
NaDCA + Dex-DCA (DS = 3%)	1.0	1.73	−2.3	–	298.15

[a] The concentrations are expressed in concentration of polymer hydrophobic side group (mol dm^{-3})

[b] Calculation based on the first injection

[c] The estimated errors are less than 6%

the titrations curves are more distant than those for pure surfactant dilution into water.

After the C_2, the observed enthalpies start to decrease, and merge into the dilution curve of the surfactant in water at about 12.5×10^{-3} mol dm^{-3}, meaning that from this concentration the added NaDS micelles are only diluted. The concentration C_2 should be the critical concentration for self-aggregation of surfactant in the presence of polymer. For all studied systems, C_2 values are only slight lower than the cmc of NaDS. This is not very surprising as we have a mixed system of a neutral polymer and a charged surfactant, where usually C_2 is not much lower than cmc. Moreover, it could also be that the hydrophobic microdomains are too tight to accommodate a large number of NaDS monomers.

Finally the aggregation enthalpies (ΔH_{agg}) in the presence of polymer can be obtained from the difference between the observed enthalpies at the two linear segments, as shown in Fig. 5. Note that the values of ΔH_{agg} are negative for all studied systems. These results are summarized in Table 2.

For comparison, calorimetric titrations for Dex-DCA (DS = 2%; C_p = 1.0 g dL^{-1}) with a cationic surfactant, DTAB was also performed, as shown in Fig. 6. We see that for the systems with DTAB the strongest interaction also takes place at very low surfactant concentration, but the interaction enthalpies (ΔH_{int}) are smaller than with NaDS (Table 2, forth column). The corresponding enthalpy of aggregation (ΔH_{agg}) in the presence of the polymer is −4.4 kJ mol^{-1} for DTAB, whereas for NaDS, $\Delta H_{agg} = -1.6$ kJ mol^{-1}. The absolute values of ΔH_{agg} are lower than the ΔH_{mic} values of pure surfactants. We can evaluate the extent of enthalpy change by calculating $\Delta = [(\Delta H_{agg} - \Delta H_{mic})/\Delta H_{mic}] \times 100$. The extent of decrease in enthalpy change is $\Delta = 18\%$ for the system Dex-DCA/DTAB and $\Delta = 70\%$ for Dex-DCA/NaDS. The association is stronger for anionic than for cationic surfactants. This result is rationalized as being due to the larger size of the cationic headgroups on the surface of the micelle [32, 52].

The curves of observed enthalpies for Dex-DCA/NaDS or DTAB are plotted as a function of the molar ratio of surfactant to hydrophobic side group ($n_s/n_{side\ group}$) in Fig. 7. This allows comparison between the different mixed systems. It is found that the molar ratios at critical concentrations related to the onset of formation of mixed micelles (C_1) do not depend on surfactant's head-group. This suggests that the polymer molecular structure has a critical effect on the aggregation behavior of these mixed systems. When the $n_s/n_{side\ group}$ ratio is low in the mixed aggregates, the aggregates are dominated by the polymer characteristics and they may be similar to the pure HMP aggregates in the absence of surfactant [37]. The molar ratios at C_2 are quite different for the two systems with different surfactants (NaDS and DTAB). The higher molar ratios at C_2 reflect the aggregation behavior of the respective pure surfactant. Clearly in this surfactant-rich

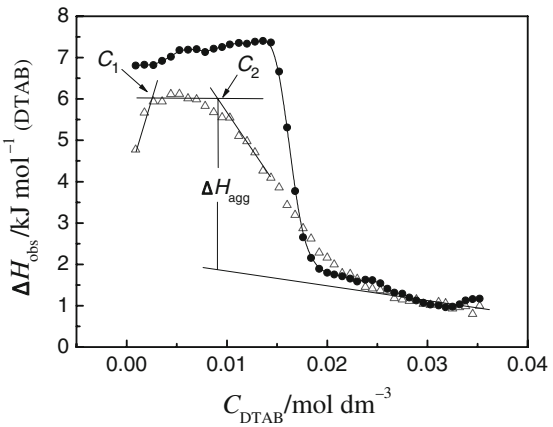

Fig. 6 Variation of the observed enthalpies with DTAB concentration for Dex-DCA (DS = 2%)/DTAB system at T = 308.15 K. Titration of DTAB (0.28 mol dm^{-3}) into pure water (●) and polymer solutions (1.0 g dL^{-1}) (Δ)

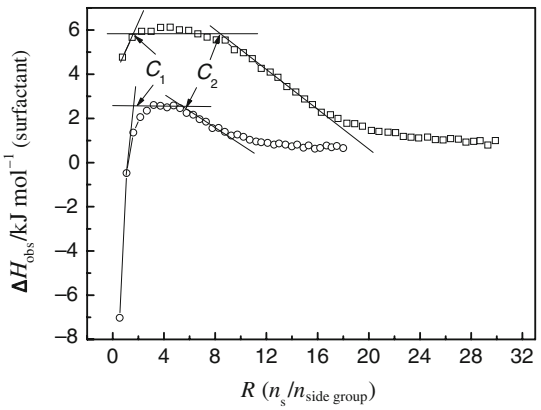

Fig. 7 Plots of observed enthalpies as function of the molar ratio of surfactant to hydrophobic side group, $R(n_s/n_{side\ group})$ at $T = 308.15$ K. (□) Dex-DCA (DS = 2%, $C_p = 1.0$ g dL^{-1})/DTAB and (○) Dex-DCA (DS = 2%, $C_p = 1.0$ g dL^{-1})/NaDS

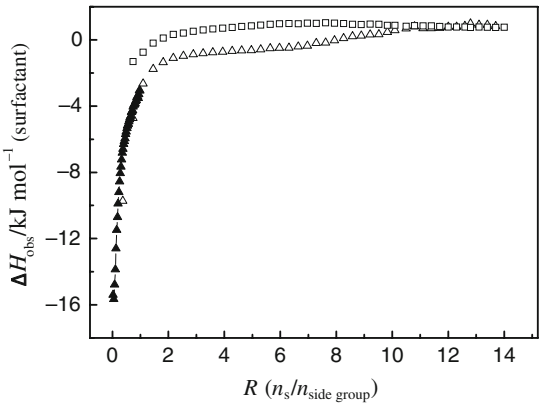

Fig. 8 Plots of observed enthalpies as function of the molar ratio of surfactant to hydrophobic side group, $R(n_s/n_{side\ group})$ at $T = 298.15$ K. (□) Dex-DCA (DS = 3%, $C_p = 1.0$ g dL^{-1})/NaDCA and (Δ) Dex-DCA (DS = 3%, $C_p = 1.0$ g dL^{-1})/NaDS. The symbols (▲) correspond to the titration curves of NaDS (0.2 mol/dm^3) into NaDCA solutions ($C_{NaDCA} = 1.0$ g dL^{-1})

region, the aggregation behavior is more and more controlled by the surfactant characteristics.

As we did consider that one important driving force in the polymer/surfactant association was the hydrophobic effect, we thought it important to complete this set of experiments with some measurements at 298.15 K. We studied the system Dex-DCA/NaDS and Dex-DCA/NaDCA. The calculated interaction enthalpies can be found in Table 2. From these, we can calculate the change in heat capacity for the interaction, obtaining -260 J K^{-1} mol^{-1}. This high and negative $\Delta C_{p,int}$ result confirms the hydrophobic contribution to the observed interaction.

In Fig. 8, we have plotted ΔH_{obs} versus $n_s/n_{side\ group}$ curves at 298.15 K for NaDCA/NaDS and Dex-DCA/NaDS or Dex-DCA/NaDCA. We can see that the interaction of the polymer with NaDCA is much weaker than with NaDS in the low concentration range. This is due to the structural features of the NaDCA surfactant, which has a rigid ring, lacking therefore the flexibility to enrol in different arrangements as NaDS hypothetically can. This can be observed quantitatively from their interaction enthalpies at $T = 298.15$ K in Table 2, i.e., the exothermic ΔH_{int} for the mixed system with NaDS is larger than one with NaDCA. Finally, we can also observe that the molar ratios at C_1 for the two systems—Dex-DCA/NaDS or NaDCA, are the same, and about equal to the values found for Dex-DCA and DTAB or NaDS at 308.15 K. This further supports our previous conclusion that at low surfactant ratio the behavior is dominated by the polymer characteristics.

Conclusions

From the calorimetric titration curves, we have obtained the enthalpies of micelle formation and critical micelle concentrations for the referred pure surfactants, as well as the interaction and aggregation enthalpies for the mixed systems- surfactant/polymer. The dependence of the observed aggregation behavior on the surfactant and temperature was discussed in detail.

The aggregation is strongly dependent on polymer structure at low $n_s/n_{side\ group}$, and on surfactant characteristics when the surfactant concentration increases. The structural characteristics of NaDCA strongly influence both the behavior of the modified polymer (Dex-DCA) with surfactants as well as its own interaction with NaDS.

As a final note, we would like to stress that calorimetry allowed us to ascertain a very important fact in polymer/surfactant interaction. From the comparison between NaDCA/NaDS and Dex-DCA/NaDS calorimetric titration curves, we can see that the interaction between Dex-DCA and NaDS is driven by the interaction between the bile acid moiety and the surfactant, because in the common measured ratios the observed curves approximately overlap (Fig. 8). Further, the obtained value for $\Delta C_{p,int}$ referred to in the discussion is about the same as the one obtained for pure NaDCA surfactant (Table 1).

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