7.1 Introduction

Mixed surfactant systems are often preferred to improve performance over single surfactant due to the synergistic interactions between oppositely charged surface-active species. The aggregate morphology results from the synergistic effects of multiple weak interactions between a large number of sub components [1].

Recently, a continuous attention has been paid to the aggregation behavior of mixed micellar systems containing bile salt and cationic surfactant [2-5]. Various interaction models with cationic surfactants are proposed in presence of NaDC [4-7]. Biological morphologies are formed by spatially matching intermolecular interactions among various constituents. However, the factors causing self-assembly and structural transitions in biological structures are poorly understood. It has been reported that bile salts mixed with steroids and phospholipids associate into helical giant morphologies. Thus, mixtures of oppositely charged amphiphilic molecules can be used as models of biological assemblies.

Micellization of NaDC on addition of surfactant has been studied much in the past [8,9]. However, there are few reports on morphological studies on CTAB - NaDC system [10, 2-4]. The nature of bile salt is also important for obtaining various microstructures in such mixtures [2,11]. A few micro-structural studies are performed on nonionic surfactant – NaDC [4], catanionic surfactant – NaDC [2] and nonionic polymer –NaDC systems [12].

NaDC is a water-soluble bile salt having good compatibility for pharmaceutical formulations [13]. NaDC is reported for the enhancement of drug permeation through biological membranes [14]. Thus, it is envisaged that mixture of NaDC and CTAB can be used as a model in pharmaceutical research for drug delivery as both components are having good water solubility. The prime objective of the present work is to get insight into morphological transitions in aqueous CTAB - NaDC system. It has been observed by visual inspection and spectro-photometrically that on addition of NaDC to aqueous CTAB solution, system turned from optically clear to viscous clear, bluish fluidic followed by phase separation. Further, more NaDC

causes again a fluidic bluish solution followed by a clear solution. Morphological transitions in the system are studied by rheology, DLS, ^{1}H NMR, polarizing microscopy and TEM. It has been reported that bile salt addition to surfactant solutions generally enhances the average head group area and causes aggregates with curved surfaces [15].

7.2 Results and Discussion

The optical data on aqueous CTAB /NaDC mixtures (Figure 1) can be divided into four regions: low OD region (I), 0 < [NaDC] < 0.03 M; medium OD region (II), 0.03 M < [NaDC] < 0.06 M; significant OD region (III), 0.06 M < [NaDC] <0.08 M, and an OD decreasing region (IV), 0.12 M < [NaDC] < 0.16 M. Further, there is one precipitation region observed roughly at equimolar concentration of CTAB and NaDC, *i.e.* 0.08 M < [NaDC] < 0.12 M. We have not studied this precipitation region. However, the distinct rise of turbidity (*e.g.* region III) with the increase in NaDC concentration suggests the growth of aggregates in the system [1, 16, 17, 18].

Similar type of OD increase was reported in oppositely charged surfactants [1] or surfactant-hydrotropic mixtures [16] and has been explained on the basis of morphological transitions (micelle ↔ cylindrical micelle ↔ vesicles). The OD data were also recorded from the sample mixtures prepared at higher pH (=9.2). Similar OD variations are observed as obtained in water (Figure 2). However, OD values were higher for the same [NaDC] indicating the presence of larger aggregates. The data (Figures 1 and 2) are in consonance with the recent work in which pH- induced morphological transitions were reported [19]. Figure 3 shows the variation of η_0 as a function of [NaDC] at fixed CTAB (0.1 M). From the comparison of Figures 1 and 3, it is clear that OD and η_0 vary in parallel as we increase the [NaDC]. The increase in η_0 implies that NaDC induces the growth of the micelles and is responsible for various morphologies in different concentration ranges (regions I-IV). η_0 reaches to a peak and thereafter drops followed by precipitation. Similar viscosity peak has been explained in the light of sphere to rod transition(s → r) [12,20].

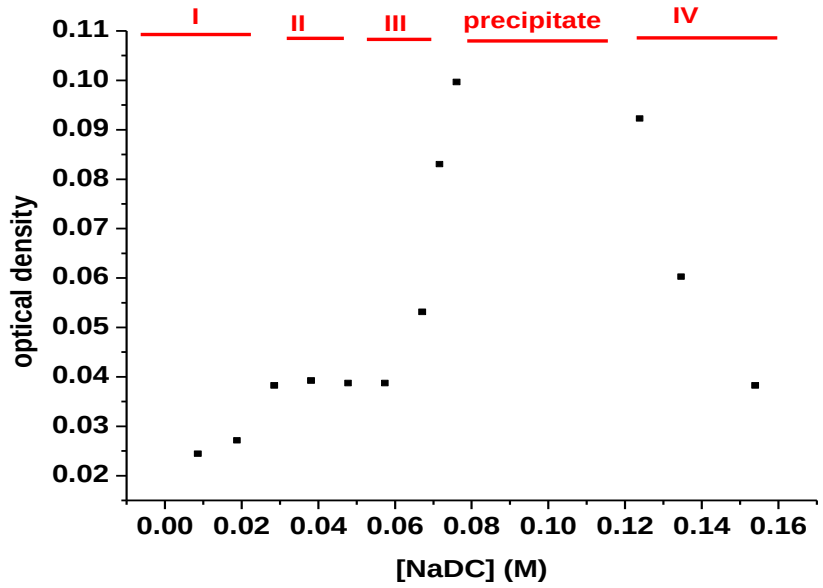

Figure 1: Variation of optical density of aqueous 0.1M CTAB with varying concentration of NaDC at 30 °C.

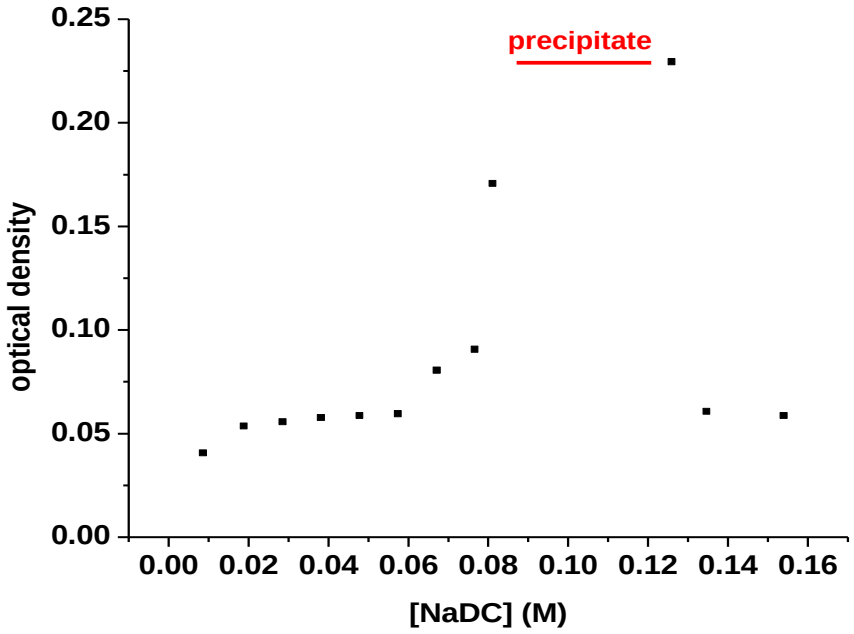

Figure 2: Variation of optical density of aqueous 0.1M CTAB (pH= 9.2) with varying concentration of NaDC at 30 °C.

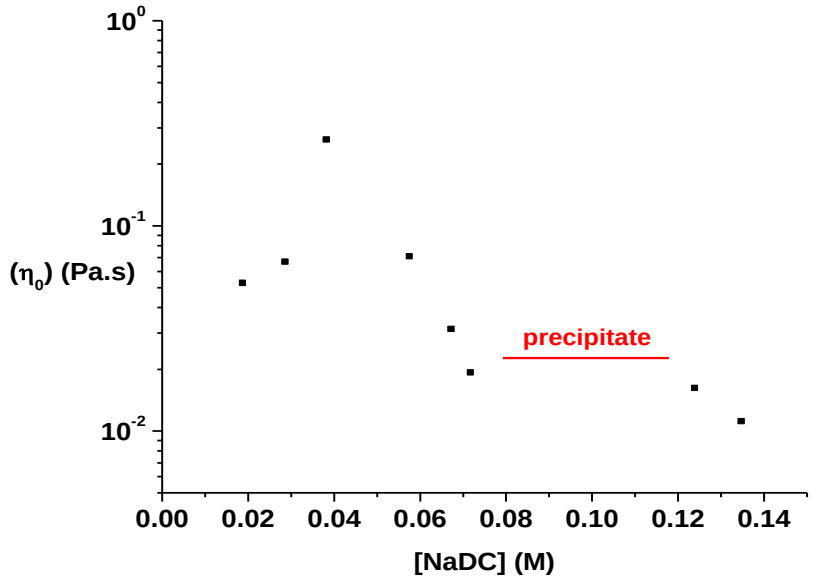

Figure 3: Variation of η_0 of aqueous 0.1M CTAB with varying concentration of NaDC at 30 °C.

After the precipitation region, η_0 decreases (so is the OD) with the further increase of [NaDC]. It should be mentioned here that sample shows a bluish hue just before the precipitation region (~0.08 M NaDC) and also after the precipitation region (~0.12 M) followed by transparent sample again with low η_0. Taken together, results (Figures 1 and 3) provide an evidence for a morphological transition to higher-order aggregates. This has been explored by conducting other experiments.

The rheological response of the CTAB - NaDC system at various [NaDC] is shown in Figure 4. We have selected representative sample of each region (of Figure 1) and shear response was seen. At low [NaDC] (0.0192 M, region I), the sample exhibits Newtonian behavior (viscosity is independent of shear rate) and the value of shear viscosity is close to that of water. This indicates that the micellar growth is not much at this concentration. At relatively higher [NaDC] (region II) (0.0382 M) sample shows a plateau in the shear viscosity at low shear rate followed by a shear thinning at higher shear rate. This rheological behavior of shear thinning can be correlated to worm like micelles in the solution. At high shear rates the viscosity drops rapidly for

the breakage of worm like micelles. At further higher concentration (0.07645 M) of NaDC(region III), the sample exhibits independence of viscosity with shear rate again. Further, this sample appears bluish in color (Figure 1). These observations allow us to propose about the presence of vesicles in the sample. The samples from region IV (0.1242 or 0.1350 M) show similar response as was observed with the sample of region III and the same morphology (vesicles) can be expected here also. Similar rheological changes have been explained in terms of micelle to vesicle transition in various surfactants - additive systems [16, 19, 21, 22]. When oppositely charged DC^- interacts with the positively charged CTAB micelles, the net surface charge on the CTAB micelles gradually reduces and thereby, a_0 responsible for decrease. This causes increase in R_p [23] with a concomitant transition in the morphologies.

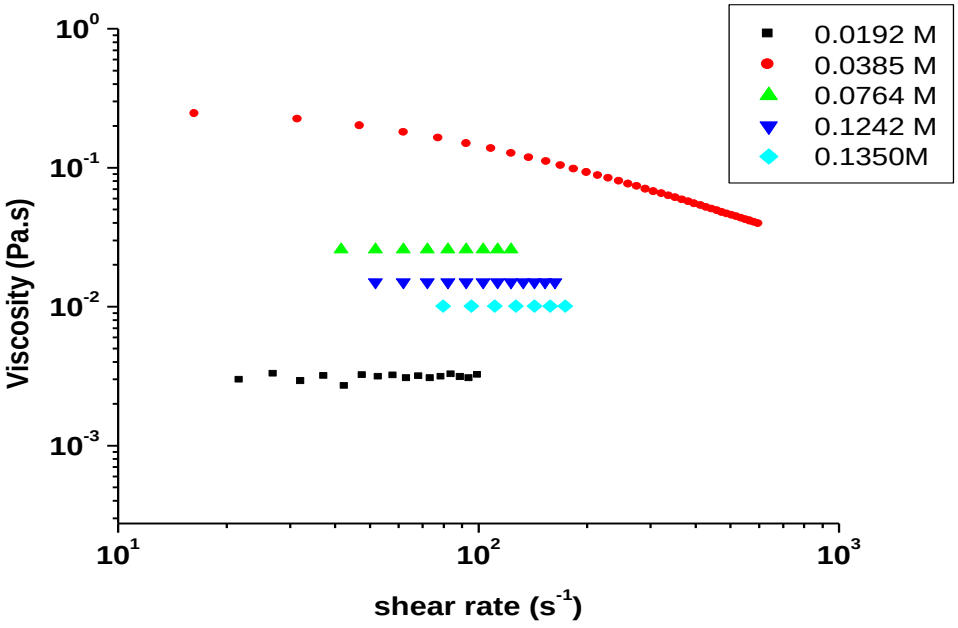

Figure 4: Variation of shear viscosity of aqueous 0.1 M CTAB with shear rate for different fixed concentrations of NaDC at 30 °C.

NaDC and CTAB are above their *cmcs* (*cmcs*, for CTAB ~ 1 mM, NaDC ~ 2.5 mM) in the mixtures studied, but our DLS data showed single peak behavior when NaDC

was added up to a fairly high concentration (Figure 5 (A – C)). However, diameter of the mixed micelle increases with the further increase of [NaDC] (Figure 5 (D – F)) which is consistent with the viscosity data (Figure 3).

Before NaDC addition, ellipsoidal micelles are expected as the major aggregates in 0.1 M pure CTAB aqueous solution. As the [NaDC] increases (region I of Figure 1), system absorbance and η_0 increases gradually together with D_h (Figure 5 (A – C)). With further addition of NaDC (0.067 M), OD shows a sharp increase indicating the bigger morphologies in the system (micellar growth) which is also seen with DLS data (Figure 4 A- C). At higher concentration (~ 0.076 M), system shows bluish appearance and maximum OD. This is consistent with the appearance of dominant single peak at ~70 nm in the DLS plot (Figure 5D). The combined results of DLS (Figure 5 (D – F)) and optical density (Figure 1) suggest that vesicles are the major aggregates in the solution (microscopic studies also support this point, *vide supra*). Further NaDC addition causes a precipitation and hampered the DLS studies. However, at 0.1242 M NaDC, again a bluish sample with an average D_h ~ 60 nm is observed (Figure 5E). More NaDC in the system (0.1543 M) resulted in to the presence of both micelles and vesicles as shown by DLS data (Figure 5F) with a decrease in vesicle size as well as the fraction in the sample. This system shows low OD (region IV, Figure 1) and η_0 (Figure 3) which is consistent with the DLS data and conversion of a few vesicles to micelle seems plausible. The present DLS data are consistent with the results obtained for vesicle to micelle transitions in the past [1, 2].

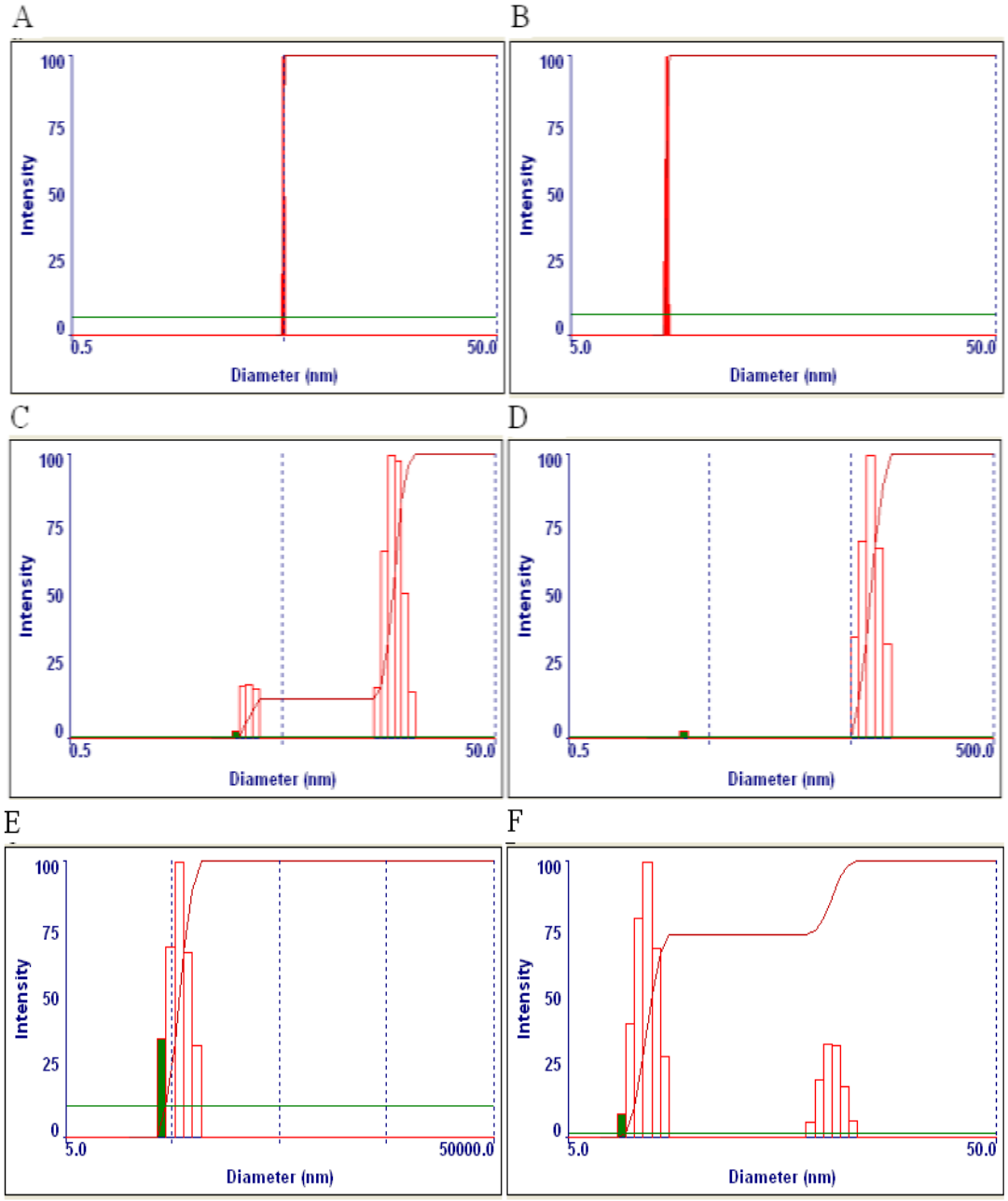

Figure 5 Size distribution profile of aggregates of aqueous 0.1M CTAB with different concentration of NaDC at 30°C (A) 0.0192 M (B) 0.0482 M (C) 0.0675 M (D) 0.07645 M (E) 0.1242 M (F) 0.1543 M.

^{1}H NMR spectroscopy has been reported as one of the convenient methods for the monitoring of changes in micellar morphology. The spectra of CTAB in D_2O at different [NaDC] are collected. Changing the solvent from H_2O to D_2O does not alter the appearance and morphology of the solutions as studied previously [17, 24, 25]. The observed δ of pure CTAB (Figure 6A) is comparable with the earlier studies [26]. The features of the spectra remain more or less same (Figure 6B) for the sample taken from region I (0.009M) indicating the similar morphology (ellipsoidal micelle) as was present with 0.1 M CTAB. NMR data show the shifting of spectra as a whole to higher δ (ppm) together with distinct broadening of the peaks as the [NaDC] increases (region II) (Figure 6C). This indicates the structural transition in the system from spherical (or ellipsoidal) micelle to rod shape micelles (or wormlike micelle). Similar peak broadening in surfactant additive systems has been explained on the basis of morphological transitions [27]. The above peak broadening decreases for the samples taken from the regions III and IV which indicates another morphological transition (rod to vesicles). It has also been proposed for oppositely charged aqueous surfactant mixtures that line broadening in NMR spectra may be due to the presence of vesicles [25]. Combining the present results with previous studies, it can be proposed that micelles together with vesicles are present in the system of different compositions (especially for regions III and IV). This can be seen from the DLS data (Figure 5). Therefore, micellar growth proposed on the basis of the previous results can be corroborated by NMR results. The NMR results hint about strong interaction between CTAB and NaDC, especially below and above the precipitation region [3].

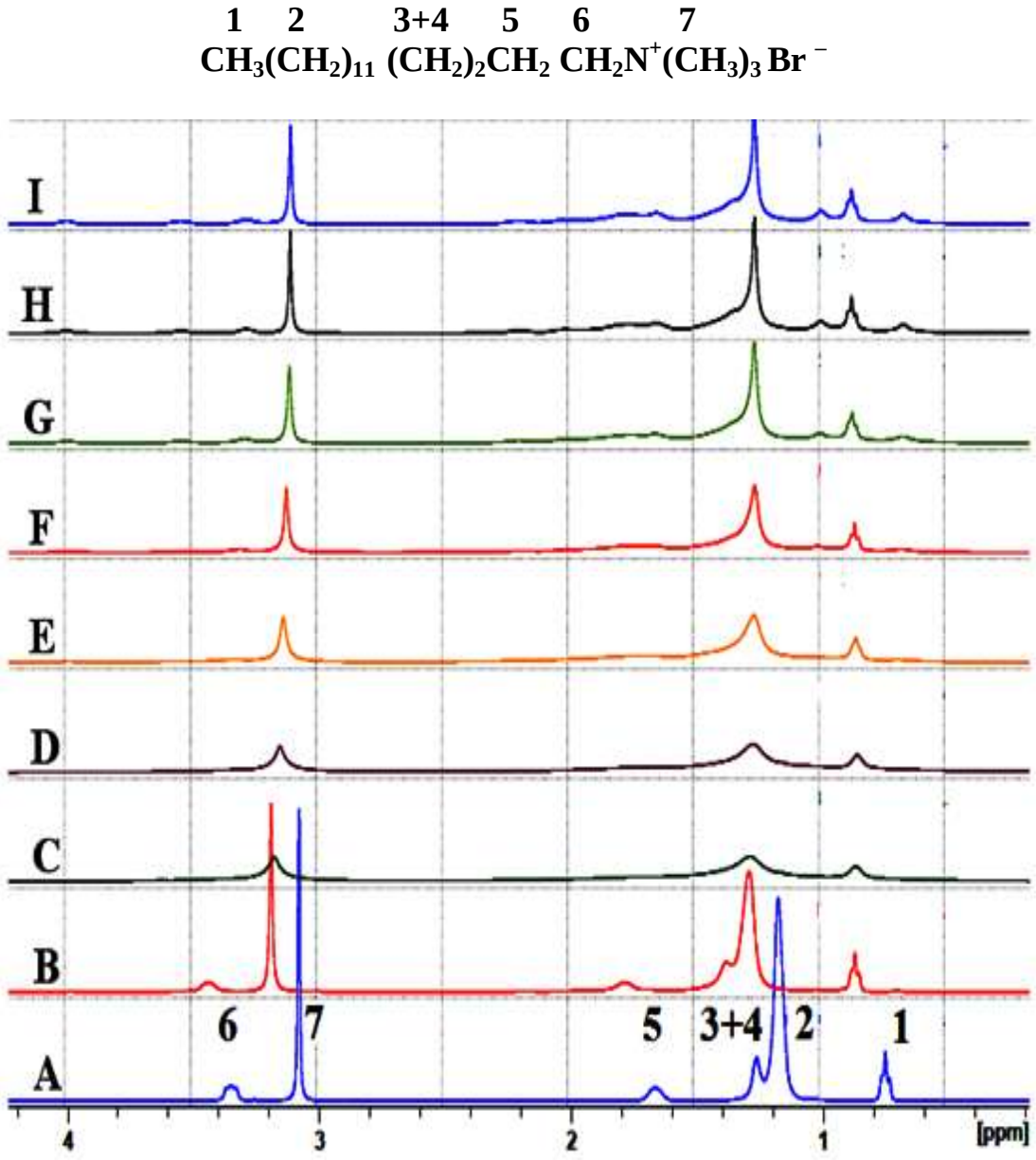

Figure 6 ^{1}H NMR spectra of aqueous 0.1 M CTAB with various NaDC concentrations; (A) pure 0.1 M CTAB (B) 0.1 M CTAB + 0.0192 M NaDC (C) 0.1 M CTAB+ 0.0289 M NaDC (D) 0.1 M CTAB + 0.0385 M NaDC (E) 0.1 M CTAB + 0.0675 M NaDC (F) 0.1 M CTAB+ 0.0764 M NaDC (G) 0.1 M CTAB + 0.1243 M NaDC (H) 0.1 M CTAB + 0.1350 M NaDC (I) 0.1 M CTAB + 0.1543 M NaDC at 30 $^{\circ}$C.

Various structural transitions take place upon addition of NaDC to CTAB solution, here two samples with [NaDC] 0.0764 M (end of region III) and 0.1242 M (start of region IV) have been chosen for polarizing microscopy. The micrographs obtained for these NaDC concentrations clearly show the presence of vesicles in the system (Figure 7).

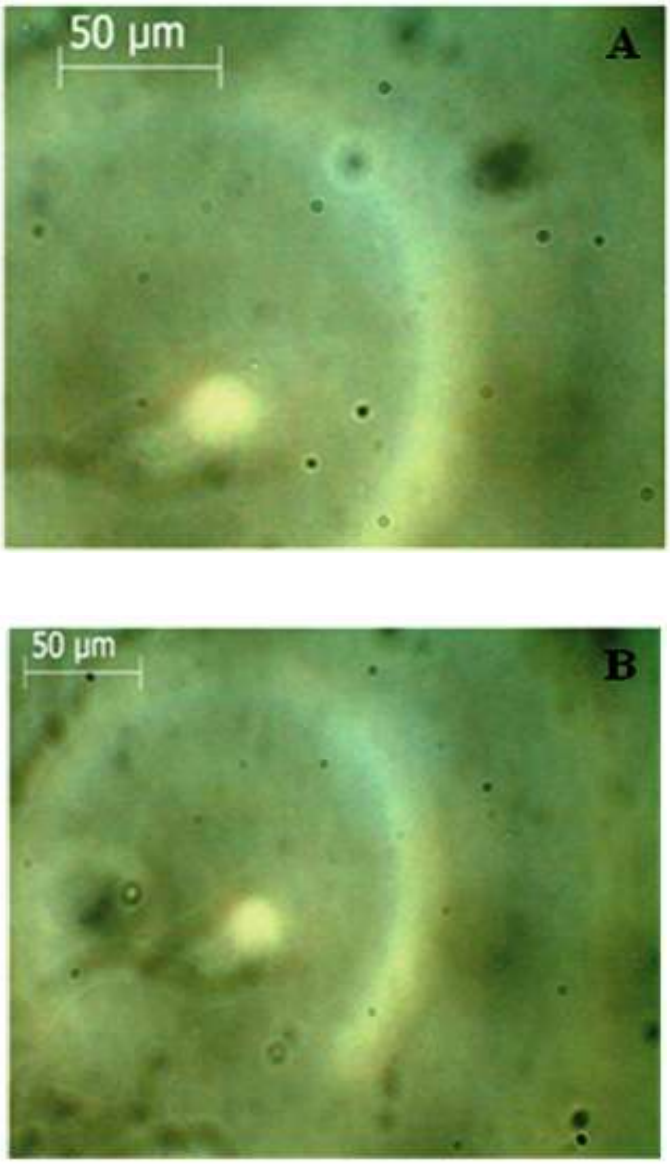

Figure 7: Optical micrographs showing the presence of vesicles in aqueous 0.1 M CTAB at NaDC concentration (A) before (0.07645 M) and (B) after (0.1242 M) precipitation.

In both the cases one can observe polydisperse vesicles. This is observed only in bluish samples and roughly at about 1: 0.75 and 1: 1.25 molar ratios of the CTAB and NaDC. For other molar ratios, most of the time, the samples were fairly clear having other micellar morphologies as indicated by DLS data. TEM images at various NaDC concentrations are shown in Figure 8. These images further support about the morphologies proposed in previous paragraphs.

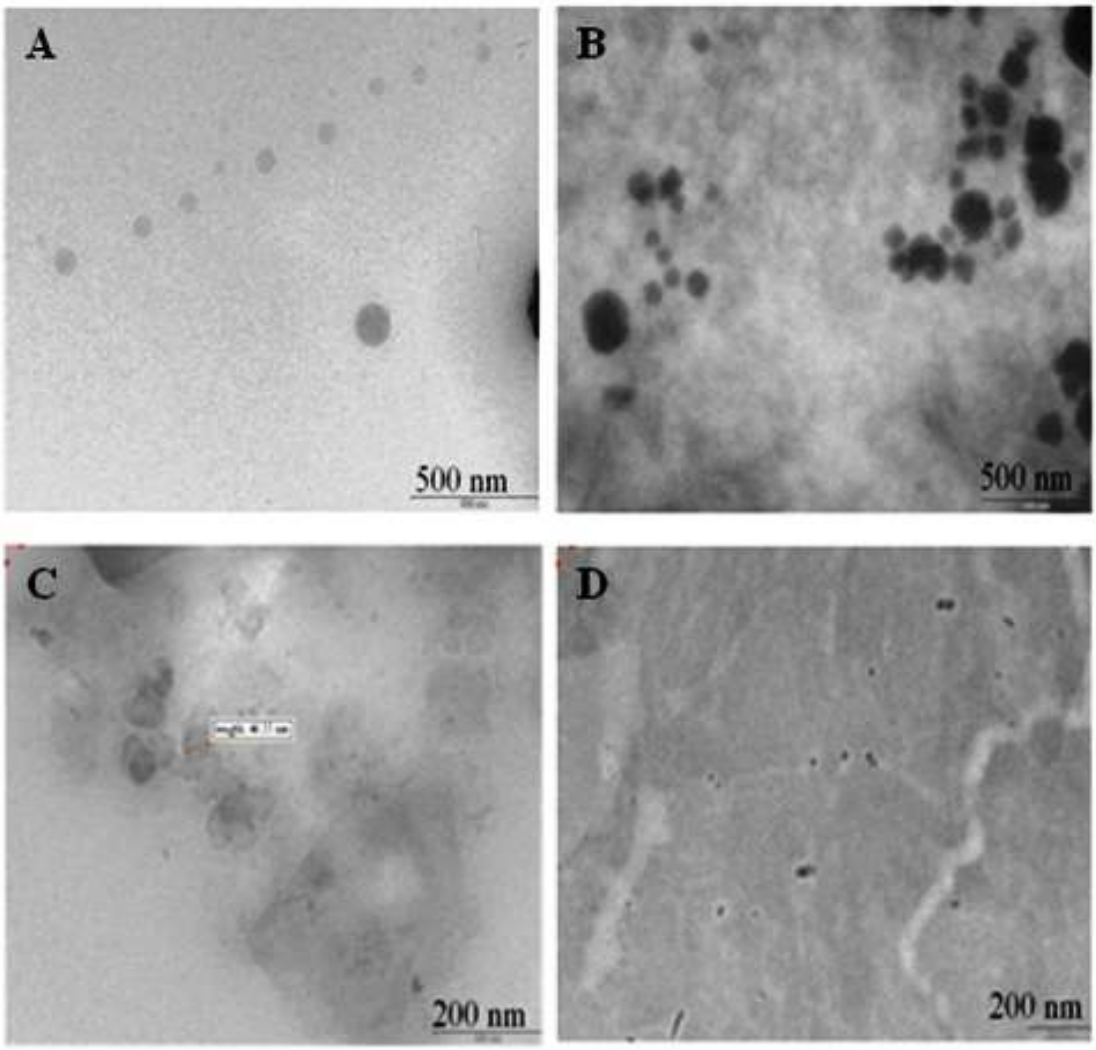

Figure 8 TEM micrographs showing the presence of vesicles in aqueous 0.1 M CTAB with various NaDC concentration (A) 0.07645 M (B) 0.1242 M (C) 0.1350 M (D) 0.1543 M.

7.2.1Effect of pH on Micellar Morphology

To get further insight, the microscopic and DLS studies have also been performed at higher pH (=9.2). Being a sodium salt of a weak acid and strong base, NaDC is expected to hydrolyze in water. At higher pH, one can expect more NaDC in the form of DC^- and Na^+. If this is correct, micelles of higher size is expected with pH = 9.2 than in pure water at same concentration of NaDC due to increased electrostatic attraction (and decrease in a_0). This indeed is observed by our turbidity (Figures 1 and 2) and DLS studies performed at [NaDC] before (Figure 9A) and after (Figure 9B) precipitation region (at pH = 9.2).

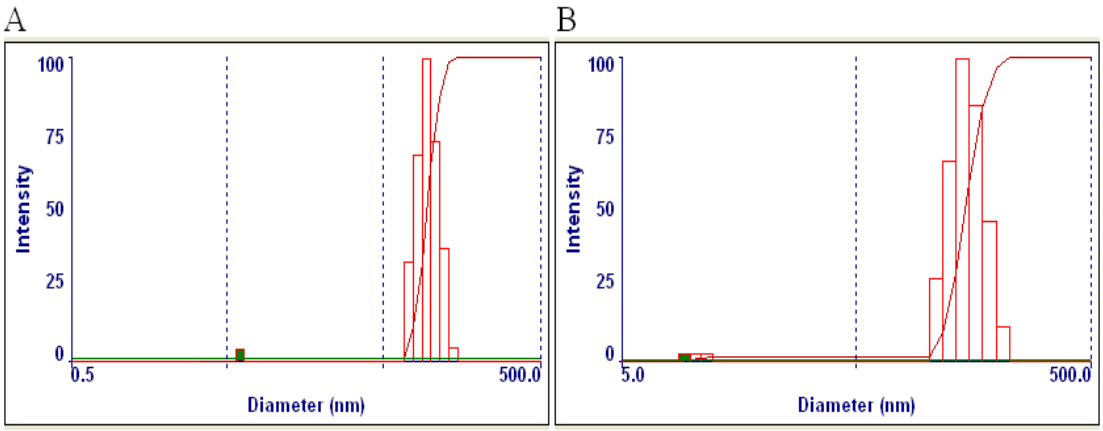

Figure 9 Size distribution profile of aggregates of aqueous 0.1 M CTAB (pH = 9.2) at NaDC concentration before (A) (0.0815 M) and (B) after (0.1263 M) precipitation at 30 $^{\circ}$C.

The mono modal size distribution with low PDI excludes the possibility of lamellar and tubular structures and hints towards spherical vesicles as confirmed by microscopic studies (Figures 10 and 11).On comparing microscopic data (Figures 7 and 10 , Figures 8 and 11), one can see that morphologies are bigger for the samples at pH= 9.2. The vesicle diameters of spherical vesicles obtained from DLS (Figure 9) and TEM micrographs (Figure 11) are in close agreement. Overall data show the importance of [NaDC] in deciding the size and morphologies of the aggregates formed in the aqueous CTAB-NaDC system.

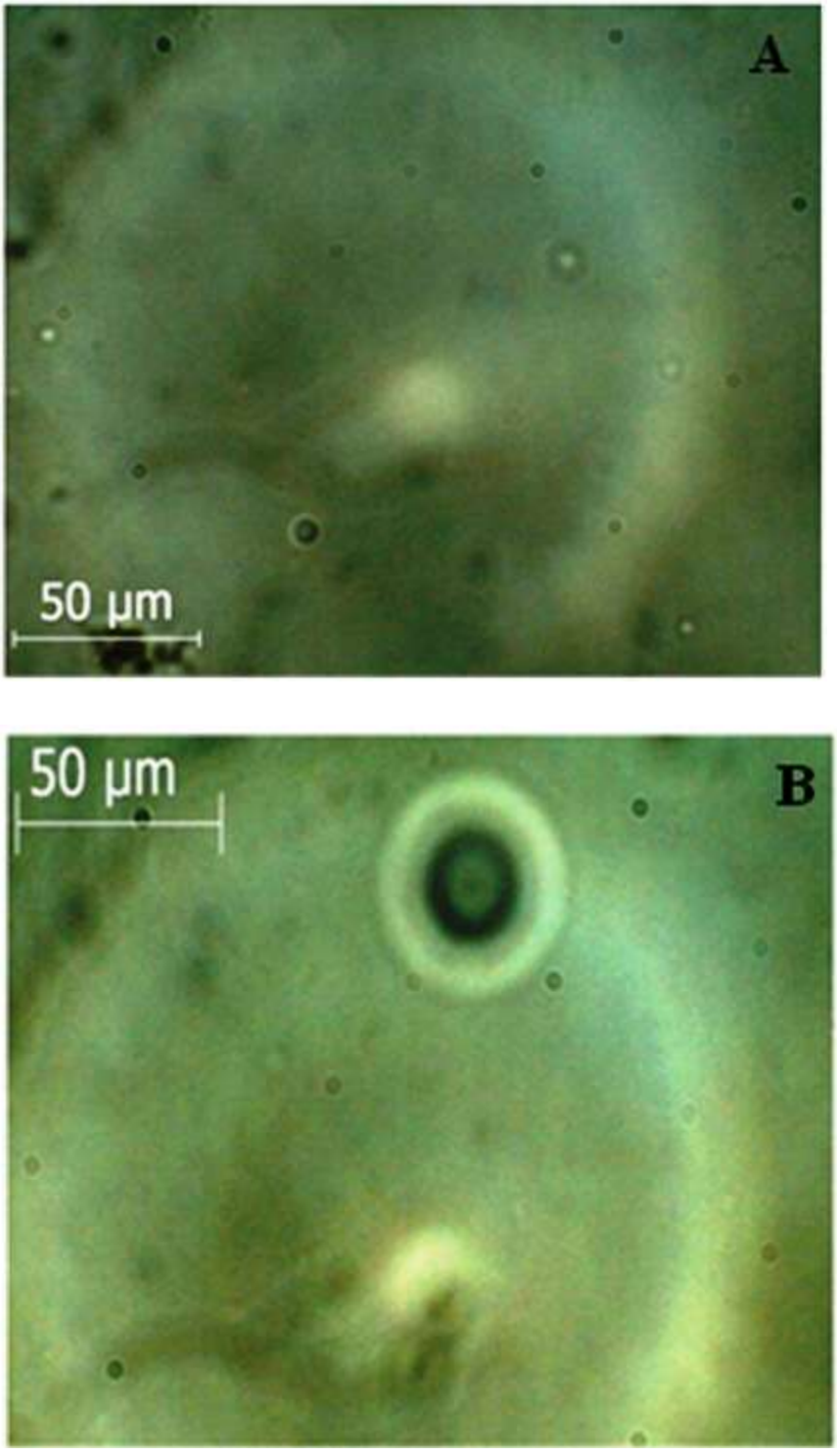

Figure 10 Optical micrographs showing the presence of vesicles in aqueous 0.1 M CTAB (pH = 9.2) at NaDC concentration (A) before (0.0815 M) and (B) after (0.1263 M) precipitation.

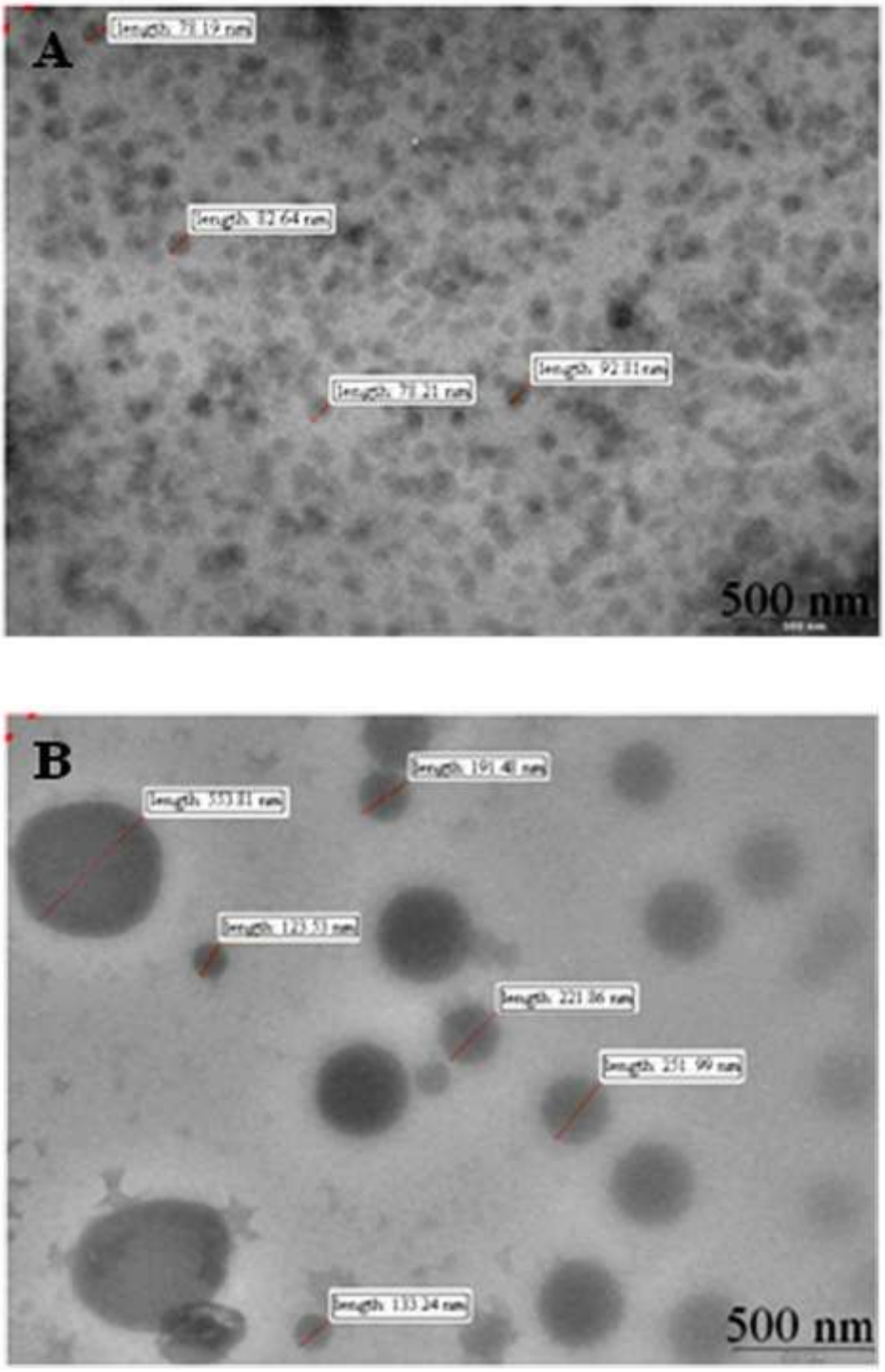

Figure 11 TEM micrographs showing the presence of vesicles in aqueous 0.1 M CTAB (pH = 9.2) at NaDC concentration (A) before (0.0815 M) and (B) after (0.1263 M) precipitation.

7.3 Conclusions

Formation of grown micelles (rod-shaped) or vesicles depends on the [NaDC] in the sample. Both microscopic and macroscopic transitions are observed on NaDC addition. The study provides the simple/effective route to design and control the morphology of self-assembled aggregates. The increase in pH of the sample shows a synergistic effect in terms of aggregate size.

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