ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Study of physicochemical properties of TTDMM dendrimer (Trimesyol-1,3,5-tridimethyl malonate) with cationic and anionic surfactants to make drug delivery system more effective

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ABSTRACT

The physicochemical properties (PCPs) like density, surface tension, viscosity, activation energy, friccohesity and molecular radii of 1st generation Trimesyol-1,3,5-trimethyl malonate (TTDMM) dendrimer with sodium dodecyl sulfate (SDS) and dodecyl trimethyl ammonium bromide (DTAB) surfactants in DMSO solvent were studied at 298.15 K and 0.1 MPa. For physicochemical properties and molecular radii of Dendrimer/Surfactant-Solvent systems 0.2, 0.4, 0.6 and 0.8 mM/L were prepared for TTDMM, SDS, DTAB in DMSO. For dendrimer-surfactant-solvent 0.2, 0.4, 0.6 and 0.8 mM/L of SDS and DTAB were prepared and mixed in 0.4mM/L solution of TTDMM in DMSO. Densities were measured by using Anton Paar Density and Sound velocity meter DSA 5000 M with $\pm 10^{-3}$ kg m^{-3} accuracy. Viscous flow time for viscosity and pendant drop numbers for surface tension were measured with Borosil-MansinghSurvismeter. The data were regressed for limiting densities, surface tension, viscosities, friccohesity, activation energies and particle size to depict SDS-TTDMM and DTAB-TTDMM binding activities. The studies revealed that the interaction of TTDMM with SDS and DTAB surfactants lead to aggregation process with hydrophilic and hydrophobic domains where SDS showed stronger interactions than DTAB. This may lead to their applications in the drug delivery systems based on the structural properties of the drug molecules for binding and releasing process. Hence, these studies may open up new windows in the field of pharmaceutical sciences.

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INTRODUCTION

Nowadays, there is thrust to investigate the physicochemical aspect of the host-guest chemistry of dendrimers with various guest molecules such as dyes, surfactants and drugs (D'Emanuele A *et al.,* 2005; Gupta U *et al.,* 2006; Cheng Y *et al.,* 2014). Dendrimers have attracted attention in recent years because of their unique structure, interesting properties and potential applications in the field of pharmaceutical sciences (Gupta S *et al.,* 2012; Kitchens K.M. *et al.,* 2005; Khandare J. *et al.,* 2012; Calderon M *et al.,* 2010). They are also being used as a substrate for attachment to antibodies and contrast agents for use in the field of biochemical and biomedical sciences (Gillies E.R *et al.,* 2002; Gupta S *et al.,* 2015). Dendrimers like PAMAM (polyamidoamine) have different surface functionalities and interior cavities which make them perfect candidates for host-guest chemistry (Esfand R *et*

al., 2001). The dendrimer-surfactant host-guest system is of great industrial and scientific importance because of its potential application in food processing, pharmaceutical, and cosmetic formulations (Wang C *et al.,* 2002; Wang C *et al.,* 2004; Ericksen B *et al.,* 2008).

In view of the diverse applications of dendrimers, it is very important to understand their interactions. Host-guest chemistry of dendrimer-surfactant has been investigated by several researchers using techniques such as Electron Paramagnetic Resonance (EPR), fluorescence probe, surface tension, viscosity, Kraft temperature, Isothermal Titration Colorimeter (ITC), Atomic Force Microscopy (AFM), ^{1}H NMR and Dynamic Light Scattering (DLS) etc. Ottaviani *et al.* have analyzed the aggregation process of ionic surfactants with PAMAM dendrimer in an aqueous medium by EPR spectroscopic studies and proposed that aggregate structures depend on dendrimer/surfactant concentration, temperature and dendrimer generation (Ottaviani M.F *et al.,* 1997; Ottaviani M.F *et al.,* 1996). Esumi *et al.* used fluorescence probe and surface tension studies and observed that carboxy and octyl end group-terminated dendrimers form dendrimer-surfactant aggregates with ionic surfactants SDS and DTAB etc. in aqueous solution (Esumi K *et al.,* 2000; Esumi K *et al.,* 2002). Bakshi *et al.* found that PAMAM dendrimer surfactant aggregates create supramolecular assemblies consisting of a dendrimer at the core and surfactant on the surface from their results based on fluorescence probe, AFM, conductivity, Kraft temperature and TEM studies (Bakshi M.S *et al.,* 2005; Bakshi M.S *et al.,* 2005). Recently, Cheng *et al.* investigated the interaction of different surfactants with a different generation of PAMAM and reported that surfactant can also penetrate the interior cavity of dendrimer depending upon the dendrimer generation, dendrimer surface functionality, surfactant concentration and surfactant charge. They further reported that dramatic change in physicochemical properties of dendrimer in the presence of surfactant is dependent on intermolecular forces (IMFs) between them (Cheng Y *et al.,* 2014; Cheng Y *et al.,* 2008; Cheng Y *et al.,* 2009).

Physicochemical properties (PCPs) are very significant for determining IMFs between dendrimer and ionic surfactants and a detailed study of PCPs could reveal valuable information on complex stability, dispersing capabilities and binding features (Singh M *et al.,* 2006; Singh M, 2014). In our earlier reports, we have studied the interactions of TTDMM dendrimer in DMSO at 298.15 K through various physicochemical properties and MTX binding and corresponding release (Tondwal R *et al.,*

2015) Further, we have sightseen the magnetic nanoparticle accumulated dendrimers (MADs) of trimesoyl-1,3,5-trimethyl malonate ester (TTDMM) as potential carrier for anticancer drugs with a sustained and controlled release tendency (Pandyaa S.R *et al.,* 2016). Considering the diverse range of host-guest interactions and drug loading/binding capacity of TTDMM dendrimers, we found that no significant study has been reported about interactions of TTDMM with ionic surfactants in solvent despite their huge potential in a variety of applications in pharmaceutical industries apart from drug delivery systems (Singh M *et al.,* 2006; Singh M, 2014; Tondwal R *et al.,* 2015; Pandyaa S.R *et al.,* 2016; Undre S.B *et al.,* 2013; Pandya S.R *et al.,* 2015; Undre S.B *et al.,* 2013).

Surfactants play a key role in making emulsions, nanoemulsions and microemulsions for effective drug delivery systems. There is a vital need to initiate an advanced understanding of TTDMM interactions with numerous surfactants. Ionic surfactants are an effective choice as ideal guests for dendrimers because of their amphiphilic nature, electrically charged polar head groups and long hydrophobic chains. To understand the interactions of TTDMM dendrimers with ionic surfactants, herein we have explored the host-guest relationship between TTDMM and ionic surfactants through various physicochemical properties of surfactant-dendrimer-solvent systems. We have chosen DTAB (dodecyl trimethyl ammonium bromide) cationic and SDS (sodium dodecyl sulfate) as anionic surfactants as both have a long hydrophobic tail of 12 carbon atoms and a hydrophilic head with positive and negative charges. Though there are several solvents which are effective DMSO was chosen as it can carry drugs across membranes and lower the risk of infection occurring whenever skin is penetrated (MacGregor W.S, 1967). It is an aprotic polar solvent with constant pH and no photonic populations were noted that could harm the structures (Rammler D.H *et al.,* 1967). In our study, we have put up our efforts to examine the interactions between the electrically charged polar head groups of surfactants (cationic DTAB/anionic SDS) with dendrimer (TTDMM) and solvent (DMSO) at 298.15 K through various physicochemical properties: surface tension, viscosity, particle size, activation energy and friccohesity.

MATERIALS & METHODS

Reagent and chemicals

Trimesoyl chloride, dimethyl malonate, sodium metal, methanol, dodecyl trimethyl ammonium bromide (DTAB), sodiumdodecylsulfate (SDS) (Sigma-Aldrich), dimethyl sulfoxide (DMSO) and ethanol (Merck India) were used as received. The

chemicals were stored overnight in vacuum desiccators filled with P_2O_5 till use. TTDMM (generation-1) dendrimer was synthesized by earlier reported procedure (Undre S.B *et al.,* 2013)

For measuring density, surface tension, viscosity, activation energy, friccohesity physicochemical properties and molecular radii of Dendrimer/Surfactant-Solvent systems 0.2, 0.4, 0.6 and 0.8 mM/L were prepared for TTDMM, SDS, DTAB in DMSO. For dendrimer-surfactant-solvent 0.2, 0.4, 0.6 and 0.8 mM/L of SDS and DTAB were prepared and mixed in 0.4mM/L solution of TTDMM in DMSO.

Instrumentation

Densities were measured by using Anton Paar Density and Sound velocity meter DSA 5000 M with $\pm 10^{-3}$ kg m^{-3} accuracy. Densimeter was calibrated with Milli-Q water. The tube was washed with acetone before and after each measurement and dried repeatedly till a persistent oscillation period was obtained, by passing dried air through a tube using an air pump. The ρ data obtained were regressed by using equation (1).

$$\rho = \rho^0 + S_\rho m \qquad (1)$$

where ρ^0 at m $\rightarrow$ 0 is the limiting density and S_ρ is the 1st-degree slope.

Viscous flow time for viscosity and pendant drop numbers for surface tension were measured with BorosilMansinghSurvismeter (cal.no. 06070582/1.01/ C-0395, NPL, India) (Singh M, 2006) at 298.15K where temperature of the unit was controlled by Lauda Alpha KA 8 thermostat with ± 0.10 K by following reported procedure (Singh M, 2006).

The viscosities were calculated from their viscous flow times (t) by using equation (2).

$$\eta = \left(\frac{t}{t_0} \right) \left(\frac{\rho}{\rho_0} \right) \eta_0 \qquad (2)$$

where, t_0 and t, ρ_0 and ρ, η_0 and η are the viscous flow time, density and viscosity of reference and liquid mixtures respectively.

Viscosity data were regressed with mM/L with equation (3).

$$\eta = \eta^0 + S_\eta m \qquad (3)$$

where η^0 at m$\rightarrow$0 is the limiting viscosity, the S_η is the 1st-degree slope for effect of composition on interaction.

The surface tension was calculated by using the following equation (4).

$$\gamma = \left(\frac{n_0}{n} \right) \left(\frac{\rho}{\rho_0} \right) \gamma_0 \qquad (4)$$

where, γ_0 and γ, ρ_0 and ρ, n_0 and n are the surface tension, density and pendant drop numbers of the reference and liquid mixture respectively.

The γ data obtained were regressed for limiting values γ^0 at m $\rightarrow$0 with equation (5).

$$\gamma = \gamma^0 + S_\gamma m \qquad (5)$$

where γ^0 is limiting surface tension and S_γ is the 1st-degree slope.

The friccohesity was calculated by using Mansingh equation (6) (Chandra A *et al.,* 2013)

$$\sigma = \sigma_0 \left[\left(\frac{t}{t_0} \pm \frac{B}{t} \right) \left(\frac{n}{n_0} \pm 0.0012 (1 - \rho) \right) \right] \qquad (6)$$

Here, σ_0 and σ, t_0 and t and n_0 and n are the friccohesity, viscous flow times and pendant drop numbers of reference and liquid mixture respectively, B/t is kinetic energy correction, $\pm 0.0012(1-\rho)$ is the buoyancy correction. The terms B/t and $0.0012(1-\rho)$ are of the order of 10^{-7}. Thus, they are omitted. Thus, Mansingh equation (6) reduces to equation (7),

$$\sigma = \sigma_0 \left[\left(\frac{t}{t_0} \right) \left(\frac{n}{n_0} \right) \right] \qquad (7)$$

Reference friccohesity was calculated from equation (8).

$$\sigma_0 = \frac{\eta_0}{\gamma_0} \qquad (8)$$

where the η_0 and γ_0 are the viscosity and surface tension of reference. The σ data were regressed at m$\rightarrow$0 with equation (9),

$$\sigma = \sigma_0 + S_\sigma m \qquad (9)$$

where σ_0 is the limiting friccohesity and S_σ is 1st degree slope.

For the determination of activation energy, the partial molal volume V_1 and V_2 for reference and solutions respectively were calculated with the following equation (10) and (11).

$$V_1 = \frac{M}{\rho} \qquad (10)$$

$$V_2 = \left[\frac{1000 \, (\rho^0 - \rho)}{m \, \rho^0 \rho} \right] + \left(\frac{M}{\rho} \right) \qquad (11)$$

where M is the molar mass, ρ_0 and ρ is the density of reference and solution respectively.

Both V_1 and V_2 were used for calculation of activation energy for the solutions (Undre S.B *et al.,* 2013) obtained from equation (12).

$$\Delta \mu_1^* = RT \ln \left(\frac{\eta_0 \, V_1}{h \, N} \right) \qquad (12)$$

Where, $\Delta\mu_1{}^*$ is the activation energy for the solvent, R is the gas constant, h is the Planck's constant, T is the temperature, η_0 is the viscosity of reference and N is the Avogadro number (6.023 x 10²³). Activation energy ($\Delta\mu_2{}^*$kJ/mol) for solutions was calculated with equation (13) (Undre S.B *et al.,* 2013), where η is the viscosity of the solution.

$$\Delta\mu_2^* = \Delta\mu_1^* - \left[\left(\frac{RT}{V_2} \right) \left((1000\eta) - (V_1 - V_2) \right) \right] \quad (13)$$

where $\Delta\mu_2{}^*$data were regressed at m→0 with equation (14),

$$\Delta\mu_2^* = \Delta\mu_2^{*0} + S_{\Delta\mu_2^*} \quad (14)$$

where, $\Delta\mu_2^{*0}$is the limiting activation energy at m→0 and $S_{\Delta\mu_2^*}$ is 1st degree slope.

The molecular radii (r) in nm were calculated with equation (15).

$$r = \sqrt[3]{\frac{3\phi}{4\pi N_A c}} \quad (15)$$

where ϕ is the volume fraction of solvent entangled with surfactant molecules, N_A is the Avogadro number, c is the concentration, π is the constant. The r data were regressed at m→0 with equation (16).

$$r = r^0 + S_r m \quad (16)$$

where r^0 is the limiting particle radii and S_r is first degree slope.

RESULT AND DISCUSSION

Density: Density is mass per unit volume or in other words, binding or holding the molecules together, so it depends upon the strength of IMFs. The densities for different systems were measured and reported in Table 1.1, Figure 2.

The trend observed from density data: SDS-TTDMM-DMSO > DTAB-TTDMM-DMSO > TTDMM-DMSO > SDS-DMSO > DTAB-DMSO, indicates that when SDS or DTAB surfactants were added to the solution of TTDMM in DMSO strong electronegative interactions develop between a charged head group of surfactant with the multifunctional groups of TTDMM. Thus, coulombic forces of attraction develop due to polarization and electrostatic interaction between dendrimer-solvent-surfactant molecules. As a result of this intermolecular distances decreases and SDS or DTAB molecules in the TTDMM-DMSO solution become densely packed compared to TTDMM-DMSO solution. Comparatively higher densities of SDS-TTDMM solutions than DTAB-TTDMM solutions may be attributed to a stronger IMFs due to higher interacting activities of polar sulfate group of SDS with the carbonyl group of TTDMM, compared to weak interaction of polar trimethylammonium group of

DTAB (Figure 1). This depicts the involvement of electronegative oxygen of the carbonyl group with the solvent DMSO as is already reported in the literature (Undre S.B *et al.,* 2013).

The increase in density with increase in the concentration of surfactants at 298.15K (Table 1.1, Figure 2) predicts a stronger solute-solvent interaction. Increasing solute concentration into the system renders more ionic moieties and multifunctional groups which lead to enhanced solute-solvent interactions.

The ρ^0 data for SDS-TTDMM-DMSO > TTDMM-DMSO, with 0.0014 kg/m³ difference, DTAB-TTDMM-DMSO > TTDMM-DMSO, with 0.0011 kg/m³ difference and SDS-TTDMM-DMSO > DTAB-TTDMM-DMSO, with 0.0003 kg/m³ difference (Table 1.2), further shows the contribution of sulfate group of SDS in developing stronger IMFs of attraction. The 0.0026 and 0.0024 kg²m⁻³mol⁻¹ slope (S_ρ) values of SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO systems respectively infer that SDS compared to DTAB shows stronger composition effect on IMFs between TTDMM and DMSO.

Viscosity: It is a flow property which depends upon the frictional forces (FFs). These frictional forces (FFs) reflect the level of IMFs, i.e. stronger the FFs, stronger will be the IMFs, and higher will be the viscosity. The viscosities of solvated solutions at 298.15 K were found in order SDS-TTDMM-DMSO > DTAB-TTDMM-DMSO > DTAB-DMSO > SDS-DMSO > TTDMM-DMSO (Table 2.1, Figure 3).

The viscosity values of SDS/DTAB-TTDMM-DMSO were found higher than those of TTDMM-DMSO at 298.15 K (Table 2.1, Figure 3). This is because of strong internal frictional/resistive force of TTDMM with SDS and DTAB surfactant molecules. If we look upon the structure of TTDMM (Figure 1), it shows void space within its structural framework and these initiate interstitial activities with ionic surfactant resulting in higher viscosity complexes with stronger IMFs. The viscous flow of such complex opposes reorientation at the outset of viscous flow which requires longer time or in other words. It exerts a high resistance during the flow via a capillary of fixed internal radii resulting in high viscosities with different composition of SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO solutions. Such surfactant-dendrimer complexes develop strong hydrophobic-hydrophilic interactions. Therefore, SDS/DTAB in TTDMM with strong IMFs of interaction produces higher viscosity. The negative charge present on sulfate group of SDS develops comparatively strong interaction with electrophilic carbonyl group present in void space of TTDMM through electrostatic forces compared to

the positive charge present on trimethylammonium group of DTAB as electronegative oxygen of carbonyl group is already involved in interactions with the solvent DMSO as shown in Figure 1. Such behaviour of surfactant could be attributed to the host-guest chemistry obtained by encapsulation of surfactant into void spaces of the dendrimer since it creates eccentricity that leads to cause torsional motion with the certain realignment of forces, rightly denoted as torsional forces. The viscosity increases with concentration (Table 2.1) because average distance between polar head of surfactants and solvent or non-polar group of surfactants and dendrimer decreases, causing strong hydrophilic-hydrophobic interactions. These strengthen the interactions of SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO with the high viscous flow.
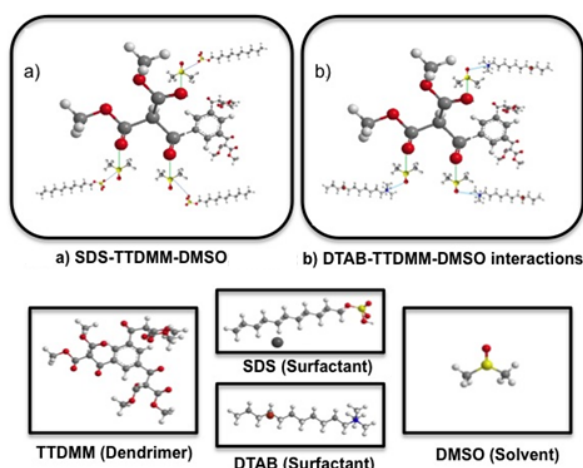

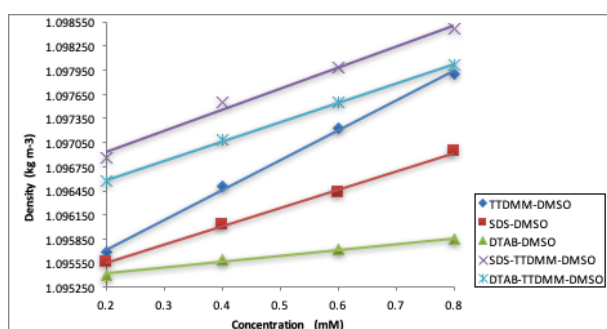Figure 1: Pictorial model showing interactions of SDS and DTAB with TTDMM in DMSO

Figure 2: Density data plots for Dendrimer, Surfactants and Surfactant-Dendrimer systems in DMSO as a solvent at a different concentration

Their limiting viscosities were calculated by using equation (3) and found to be SDS-TTDMM-DMSO > DTAB-TTDMM-DMSO > TTDMM-DMSO (Table 2.2, Figure 3).

The 0.0409 and 0.291 mPa.s kg mol^{-1} slope values of viscosities for SDS-TTDMM-DMSO solutions and DTAB-TTDMM-DMSO solutions, respectively reflects stronger composition effect with SDS-TTDMM-DMSO than DTAB-TTDMM-DMSO by a

factor of 1.405 times (Table 2.2). This data supports strong interaction of negatively charged polar head groups of SDS as compared to positively charged polar head groups of DTAB with TTDMM in DMSO. However, slopes for both the systems i.e. SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO are positive which infer structure breaking effect. The difference in η^0 data are as follow:

$\Delta \eta^0$ = (SDS-TTDMM-DMSO)-(TTDMM-DMSO)= 2.0055 -1.9539mPa.s = 0.0516 mPa.s

$\Delta \eta^0$ = (DTAB-TTDMM-DMSO)-(TTDMM-DMSO)= 1.9968-1.9539mPa.s = 0.0429 mPa.s

$\Delta \eta^0$ = (SDS-TTDMM-DMSO)-(DTAB-TTDMM-DMSO)=2.0055-1.9968mPa.s= 0.0087 mPa.s

Thus, SDS-TTDMM-DMSO shows 0.0516 mPa.s and DTAB-TTDMM-DMSO shows 0.0429 mPa.s more η^0 than TTDMM-DMSO while SDS-TTDMM-DMSO shows 0.0087 mPa.s more η^0 than DTAB-TTDMM-DMSO.
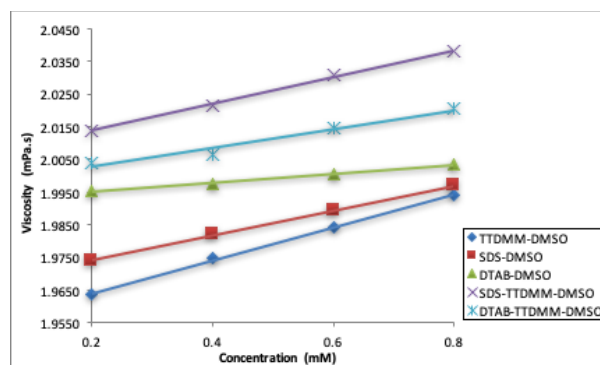

Figure 3: Viscosity data plots for Dendrimer, Surfactants and Surfactant-Dendrimer systems in DMSO as a solvent at a different concentration
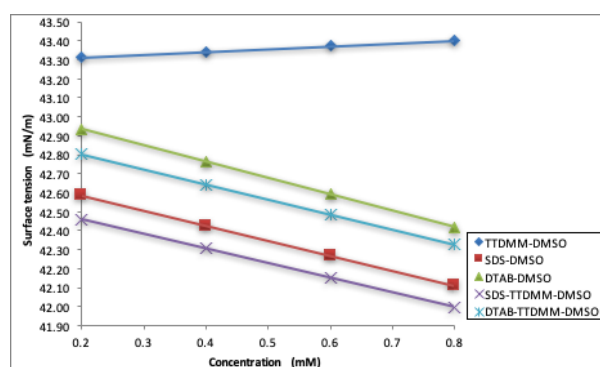

Figure 4: Surface tension data plots for Dendrimer, Surfactants, and Surfactant-Dendrimer systems in DMSO as a solvent at different concentrations

Surface tension: It is a cohesive property, which reflects upon the level of IMFs responsible for interaction between the molecules of the colloidal solution. Therefore, in this context stronger are the cohesive forces, higher is the surface tension.

Table 1: Density (ρ ± 10³ kg.m⁻³) values for different concentrations of Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent systems at 298.15 K

Concentration (*mM/L*)	TTDMM-DMSO (*ρ*)	SDS-DMSO (*ρ*)	DTAB-DMSO (*ρ*)	SDS-TTDMM-DMSO (*ρ*)	DTAB-TTDMM-DMSO (*ρ*)
0.2	1.095680	1.095565	1.095401	1.096865	1.096570
0.4	1.096508	1.096018	1.095586	1.097543	1.097086
0.6	1.097221	1.096426	1.095715	1.097986	1.097556
0.8	1.097907	1.096935	1.095845	1.098465	1.098015

Table 2: Limiting Density (ρ°, kg m-3) values for Dendrimer-Solvent, Surfactant-Solvent, Surfactant-Dendrimer-Solvent systems at 298.15 K

	TTDMM-DMSO	SDS-DMSO	DTAB-DMSO	SDS-TTDMM-DMSO	DTAB-TTDMM-DMSO
Limiting density (*ρ°*, kg m⁻³)	1.0950	1.0951	1.0953	1.0964	1.0961
1ˢᵗ slope (*S_ρ*, kg²m⁻³mol⁻¹)	0.0037	0.0023	0.0007	0.0026	0.0024

Table 3: Viscosity (η ± 10⁻⁵ mPa.s) values for different concentrations of Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

Concentration (*mM/L*)	TTDMM-DMSO (*η*)	SDS-DMSO (*η*)	DTAB-DMSO (*η*)	SDS-TTDMM-DMSO (*η*)	DTAB-TTDM M-DMSO (*η*)
0.2	1.9636	1.9740	1.9951	2.0138	2.0039
0.4	1.9747	1.9819	1.9976	2.0215	2.0065
0.6	1.9843	1.9891	2.0006	2.0306	2.0144
0.8	1.9942	1.9971	2.0035	2.0380	2.0206

Table 4: Limiting Viscosity (η°, mPa.s)values for Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent systems at 298.15 K

	TTDMM-DMSO	SDS-DMSO	DTAB-DMSO	SDS-TTDMM-DMSO	DTAB-TTDMM-DMSO
Limiting Viscosity (η°, mPa·s)	1.9539	1.9664	1.9922	2.0055	1.9968
1ˢᵗ slope (S_η, mPa·s kg m⁻¹)	0.0507	0.0382	0.0140	0.0409	0.0291

Table 5: Surface tension (γ ± 10⁻²mNm⁻¹) for different concentrations of Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

Concentration (*mM/L*)	TTDMM-DMSO (*γ*)	SDS-DMSO (*γ*)	DTAB-DMSO (*γ*)	SDS-TTDMM-DMSO (*γ*)	DTAB-TTDMM-DMSO (*γ*)
0.2	43.31	42.58	42.94	42.46	42.80
0.4	43.34	42.42	42.76	42.31	42.64
0.6	43.37	42.27	42.59	42.15	42.48
0.8	43.40	42.11	42.42	42.00	42.33

The surface tension data of these compounds depicts that the ionic surfactant weakens the surface tension of the medium due to more interactions which may be at the air-liquid interface. Probably, the surfactant interacts with the medium strongly due to ion-dipole interactions that may weaken the electrostatic interaction of the medium so that the tension is reduced. When the liquid mixtures of these compounds were subjected for surface tension (γ) measurements, the data of surface tension was found as TTDMM-DMSO > DTAB-DMSO > DTAB-TTDMM-DMSO > SDS-DMSO > SDS-TTDMM-DMSO (Table 3.1, Figure 4).
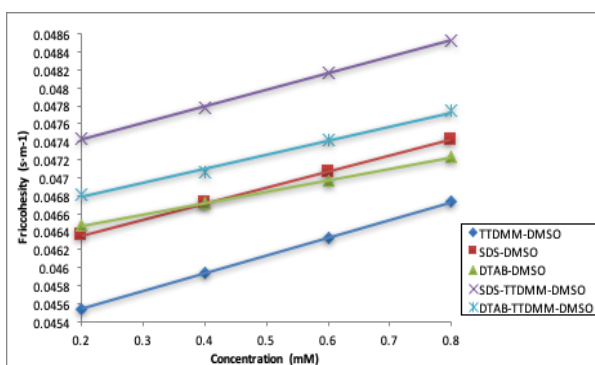

Figure 5: Friccohesity data plots for Dendrimer, Surfactants, and Surfactant-Dendrimer systems in DMSO as a solvent at different concentrations

Table 6: Limiting surface tension (γ°, mNm⁻¹) values for Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

	TTDMM-DMSO	SDS-DMSO	DTAB-DMSO	SDS-TTDMM-DMSO	DTAB-TTDMM-DMSO
Limiting surface tension ($\gamma°$, mN m⁻¹)	43.28	42.74	43.1	42.61	42.96
1st slope (S_γ, mN kg mol⁻¹m⁻¹)	0.146	-0.79	-0.86	-0.77	-0.79

Table 7: Friccohesity (σ, s.m⁻¹) values for different concentrations of Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

Concentration (*mM/L*)	TTDMM-DMSO (σ)	SDS-DMSO (σ)	DTAB-DMSO (σ)	SDS-TTDMM-DMSO (σ)	DTAB-TTDMM-DMSO (σ)
0.2	0.045530	0.0463555	0.046468	0.047430	0.046817
0.4	0.045946	0.046716	0.046714	0.047780	0.047054
0.6	0.046333	0.047063	0.046973	0.048175	0.047415
0.8	0.046730	0.047424	0.047232	0.048528	0.047739

Table 8: Limiting friccohesity (σ⁰, s.m⁻¹) values for Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

	TTDMM-DMSO	SDS-DMSO	DTAB-DMSO	SDS-TTDMM-DMSO	DTAB-TTDMM-DMSO
Limiting friccohesity (σ^0, s.m⁻¹)	0.045139	0.046001	0.046209	0.047057	0.046474
1st slope ($S\sigma$, s.m⁻¹.kg²mol²)	0.001992	0.001777	0.001275	0.001844	0.001564

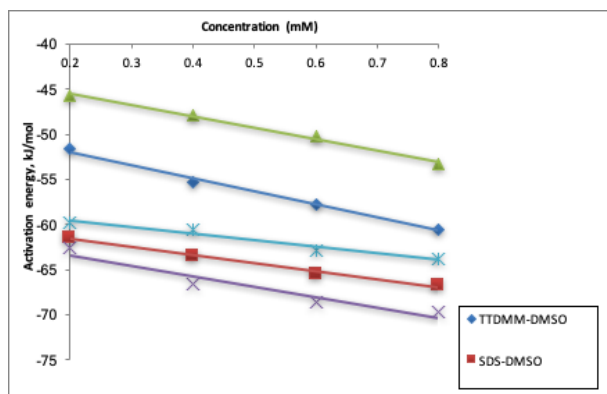**Figure 6: Activation energy data plots for Dendrimer, Surfactants, and Surfactant-Dendrimer systems in DMSO as a solvent at different concentrations**
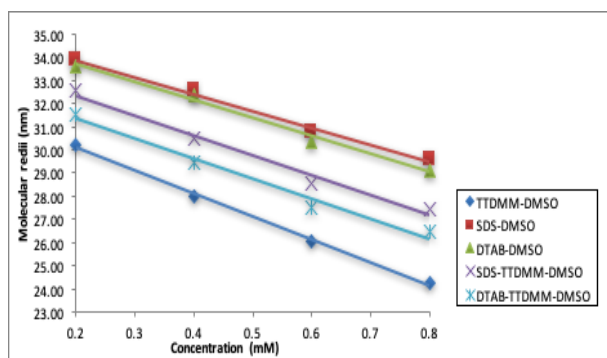

Figure 7: Molecular radii data plots for Dendrimer, Surfactants, and Surfactant-Dendrimer systems in DMSO as a solvent at different concentrations

The behaviour of SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO solution shows lower surface tension at higher composition while TTDMM shows higher surface tension at higher concentration (Figure 4). In the case of TTDMM, strong IMFs develop with dipole-dipole interaction between carbonyl group of TTDMM and sulphonyl group of DMSO. However, when surfactants with charged head groups are added, they replace DMSO molecules that interact with TTDMM causing the weakening of IMFs leading to a decrease in surface tension values. DTAB has less interacting capacity with the carbonyl group of TTDMM because of its strong interaction with DMSO as explained and supported by viscosity and density data, so DTAB-TTDMM-DMSO solutions have higher surface tension than SDS-TTDMM-DMSO solutions. More the surfactant molecules are added, more they replace DMSO molecules. Thus, when surfactant molecules are increased, there is an increase in surfactant-solvent-surfactant interactions, where the surface energy associated with adhesive and cohesive forces is neutralized in such reorientation of surfactant-solvent-surfactant molecules that produce lower surface tension with the composition of surfactant. Surface tension depicts cohesive forces in similar molecules, while the viscosity depicts IMFs in dissimilar molecules. Thus, surface tension is lower and viscosities are higher for the surfactant-dendrimer-solvent system than dendrimer-solvent

Table 9: Activation energy ($\Delta\mu$*2 ± 10-2 kJmol-1) values for different concentrations of Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

Concentration (mM/L)	TTDMM-DMSO ($\Delta\mu^{*}_{2}$)	SDS-DMSO ($\Delta\mu^{*}_{2}$)	DTAB-DMSO ($\Delta\mu^{*}_{2}$)	SDS-TTDMM-DMSO ($\Delta\mu^{*}_{2}$)	DTAB-TTDMM-DMSO ($\Delta\mu^{*}_{2}$)
0.2	-51.67	-61.45	-45.67	-62.65	-59.78
0.4	-55.34	-63.57	-47.87	-66.54	-60.65
0.6	-57.78	-65.57	-50.15	-68.56	-62.95
0.8	-60.56	-66.84	-53.28	-69.76	-63.78

Table 10: Limiting activation energy ($\Delta\mu$*$_2$⁰, kJ mol-1) values for Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

	TTDMM-DMSO	SDS-DMSO	DTAB-DMSO	SDS-TTDMM-DMSO	DTAB-TTDMM-DMSO
Limiting activation energy ($\Delta\mu^{*}_{2}{}^{0}$, kJ mol-1)	-49.06	-59.81	-42.97	-61.07	-58.22
1st slope ($S_{\Delta\mu^{*}_{2}}$, kJ L/mM²)	-14.56	-9.07	-12.56	-11.68	-7.15

Table 11: Molecular radii (r, nm) values for different concentrations of Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

Concentration (mM/L)	TTDMM-DMSO (r)	SDS-DMSO (r)	DTAB-DMSO (r)	SDS-TTDMM-DMSO (r)	DTAB-TTDMM-DMSO (r)
0.2	30.18	33.85	33.63	32.57	31.56
0.4	27.99	32.55	32.39	30.46	29.46
0.6	26.02	30.76	30.35	28.56	27.53
0.8	24.24	29.56	29.13	27.46	26.46

Table 12: Limiting molecular radii (r⁰, nm) values for Dendrimer-Solvent, Surfactant-Solvent, and Surfactant-Dendrimer-Solvent at 298.15 K

	TTDMM-DMSO	SDS-DMSO	DTAB-DMSO	SDS-TTDMM-DMSO	DTAB-TTDMM-DMSO
Limiting molecular radii (r^{0}, nm),	32.09	35.35	35.26	34.07	33.06
1st slope (S_r, nm)	-9.9	-7.34	-7.78	-8.61	-8.61

system (Figure 3 and Figure 4). The limiting surface tension (γ^{0}) calculated by equation (5) were found as 43.28, 42.96 and 42.61mN/m, TTDMM-DMSO > DTAB-TTDMM-DMSO > SDS-TTDMM-DMSO (Table 3.2), which proves that surfactant weakens the cohesive forces.

Friccohesity: It is a dual force theory and is measured to be the result of frictional forces (FFs) and cohesive forces (CFs) within similar or dissimilar molecules (Singh M, 2016). The cohesive forces occur among the TTDMM molecules and the surfactant molecules when they interact with each other. When cohesive forces weaken, frictional forces start to develop at the same level, and hence, these are interconnected forces. The strength of FFs and CFs reveal the state of interaction between surfactant-dendrimer molecules. The friccohesity values increase with an increase in the concentration of

SDS and DTAB in TTDMM-DMSO solution (Table 4.1, Figure 5).

The high friccohesity of SDS-TTDMM-DMSO system infers the strong interconversion of CFs to FFs due to higher interactions of SDS molecules with a larger surface area of TTDMM (Undre S.B *et al.,* 2013). This leads to strong FFs and weak CFs due to strong surfactant-dendrimer entanglement as was also confirmed by their higher viscosities and lower surface tension values (Figure 3 and 4). The reduced values of friccohesity of DTAB-TTDMM-DMSO illustrate weak interactions due to weak FF between DTAB and TTDMM molecules as already explained. The limiting friccohesity of SDS-TTDMM-DMSO system (0.047057 s.m-1) is higher by 0.000583 s.m-1 as compared to the DTAB-TTDMM-DMSO system (0.046474 s.m-1) (Table 4.2, Figure 5). The slopes of friccohesity *vs* different concentration of SDS-TTDMM-DMSO and DTAB-

TTDMM-DMSO also confirms the structural interacting mechanism moderated through hydrophobic and hydrophilic domains as shown in Table 4.2, Figure 1.

Activation energy: It is the minimum amount of energy required to initiate a chemical reaction and interaction process. The activation energy for liquid mixture indicates the involvement of a larger number of molecules inducing collision to facilitate solute-solvent interaction. For example, activation energies were found negative for all the system (Table 5.1) and the $\Delta\mu_2^* < 0$ infers that TTDMM and surfactant dissolution is spontaneous. The activation energies ($\Delta\mu_2^*$) for surfactant-dendrimer systems were found in order SDS-TTDMM-DMSO > DTAB-TTDMM-DMSO > TTDMM-DMSO (Table 5.1, Figure 6).

This trend indicates that SDS-TTDMM-DMSO system has the highest spontaneity for interaction because the dipolar DMSO and electrostatic structure of water induce interacting tendency in TTDMM and SDS and hence in this context component like surfactant and dendrimers get activated for developing structural interaction. SDS-TTDMM-DMSO system shows stronger interaction with a higher value of activation energy while DTAB-TTDMM-DMSO system develops comparatively weaker interaction with lower activation energy. Limiting activation energy ($\Delta\mu_2^{*0}$) for SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO solutions were found as -61.07 and -58.22 kJ/mol respectively (Table 5.2). The higher value of $\Delta\mu_2^{*0}$ for SDS-TTDMM-DMSO by 2.85 kJ/mol depicts more electrostatic forces of attraction in this case.

Molecular Radius: The molecular radius plays an important role in the study of hydrophilic and hydrophobic interacting activities. In our systems, the molecular radii change with a change in concentration or by changing surfactant. This infers that surfactant-dendrimer molecular system enhances the structural activities. The molecular radii decrease with an increase in concentration from 0.2 mM/L to 0.8 mM/L (Table 6.1 and Figure 7).

The molecular radii with 1.01 nm difference in case of SDS-TTDMM-DMSO and DTAB-TTDMM-DMSO infer cage formation of SDS, which may produce higher molecular radii which are also confirmed by their densities, viscosities, surface tension, activation energy and friccohesity studies.

CONCLUSIONS

The physicochemical properties of SDS-TTDMM and DTAB-TTDMM interactions were mainly determined by a combination of ionic interactions and hydrophobic-hydrophilic interactions. The interaction/binding of SDS and DTAB surfactants with TTDMM dendrimer depends on surfactant concentration, nature of the polar head of surfactant and structural properties of the dendrimer. The dimethyl malonate ester surface terminated TTDMM dendrimer are capable to bind with surfactants due to a higher number of binding sites and the accommodating capability.

Among the present surfactants, DTAB has weaker while SDS has higher interactions with TTDMM. The physicochemical properties determine the structural interacting potential with dimethyl malonate ester terminated surface groups of TTDMM which produce electropositive character. This may lead to their applications in the drug delivery systems based on the structural properties of the drug molecules for binding and releasing process. Hence, these studies may open up new windows in the field of biomedical and biochemical sciences.

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