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Molecular Interactions of First and Second Tier Dendrimers, Anticancer Molecules, Analyzed with Densities and Viscosities of Their Aqueous Mixtures

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Abstract

Densities and viscosities of Tridiethymalonatetriazine (2,4,6) (TDEMTA) 1st (G_1) and Hexadiethylmalonatetriazine (2,4,6) (HDEMTA) 2nd (G_2) tier dendrimers for 0.62 to 10 mg % aqueous solutions are reported at 298.15 K and 303.15 K temperatures. Their data were compared with those of Trichlorotriazine (TCT), Triacetotrizine (TAT) and Trihydroxytrizine (THT) used as markers in the study. The densities for G_2 are higher values than of G_1 but both the dendrimers showed higher densities than those of the solvent with stronger heteromolecular forces due to stronger solvation and Intramolecular multiple force theory (IMMFT).

***Keywords**: Activation energy, intrinsic viscosity, frequency factor, dendrimer.*

Introduction

Study on TDEMTA and HDEMTA are reported in earlier work[1] and densities and viscosities are reported in this paper. Dendrimers are a new class of polymeric materials. They are highly branched, monodisperse macromolecules. Structural advantages allow dendrimers to play important role in the field of nanotechnology, pharmaceutical and medicinal chemistry with specific intramolecular multiple force theory (IMMFT) and T-entropy. As a result of their unique behaviour dendrimers are suitable for wide range of biomedical and industrial applications[2]. In 2000, Cagin et al. described some recent developments in the area of dendrimers and molecular modeling applications in nanoscale[3]. The molecules showed peculiar physicochemical properties that may be targeted for nanotechnological uses[1,4]. The molecules contain central part noted as core and branching or chains with functional end groups propagate on core for further bifurcation of the chains[5, 6] in multiple of 2n. The n may be 1, 2, then number of bifurcation occur accordingly, the n is times of bifurcation[7] which is even number.

The dendrimer is divided into (a) initial core (b) inner branching unit (c) end groups with stronger networking[8-10] with larger surface area[9-12] and significant void spaces inside molecules.

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It forms many channels and cavities[12, 13] to trap foreign material like boron neutron capture therapy[14] and many others[9, 14-17] in medical sciences, drug delivery systems, biomedical, biophysical, and biochemical[9,18] fields using friccohesity, a dual force theory (DFT) with respect to chiral friccohesity. The molecules are biodegradable in nature with respect to polar solvent[1] and also ecofriendly. Their synthesis goes back to 1978, when Fritz Vogtle and coworkers first synthesized a dendrimer by Michael addition of acryonitrile to a primary amine ($-NH_2$) group followed by reduction of a nitrite ($-NO_2$) group to amine(cascade synthesis)[15, 20,22,24,30]. In 1985, Donald A. Tomalia synthesized polyamidoamine(PAMAM)[7,10,31] with no physical data.[21] The dendrimers are of great significance [22] but limited studies on them are cited. However our data are very informatory to further widen their applications.[23-29] The dendrimers do have stronger CBF (covalent bonding force) and ESF (electrostatic force) which facilitate interacting mechanism.

Experiments Methods

For densities and viscosities, Millipore water was used for solutions, w/w with better accuracy than ± 0.01 mg. The molecules were stored in a P_2O_5 filled dessicator. The densities were obtained with bicapillary pyknometer[23-24] and viscosities with Borosil Mansingh Survismeter (catalogue no.3453).[26, 27] The solutions were thermostated with ± 0.05 K control. Standard errors in data were analyzed and were to a level of $\pm 5x10^{-2}$ kg m^{-3}. The water densities were taken from literature.[26]

Results

Densities ρ were calculated with usual equations[27] with buoyancy correction for air. The ρ data with conc. c in % were fitted into a polynomial equation 1.

$$\rho = \rho^0 + S_d\, c + S_d'c^2 \qquad (1)$$

The ρ^0 is extrapolated value at $c \rightarrow 0$ and denote limiting density, S_d and $\underline{S_d}'$ are slopes, given in Tables 1. Their experimental densities are plotted in Fig.1. The viscosities were fitted into an extended Jones-Dole equation[23] given below.

$$(\eta_r\text{-}1)/c = B + Dc + D'c^2 \qquad (2)$$

Table 1: *Limiting densities $\rho^0/10^3 kg\ m^{-3}$, with 1st and 2nd-degree slope values, $S_d/10^3 kg^2\ m^{-3} mol^{-1}$ and $S_d^*/10^3 kg^4\ m^{-3} mol^{-3}$, on a regression of ρ data with c %.*

Systems	Temperature (K)	ρ^0	S_d	S_d^*
G_1 dendrimer	298.15	0.9967	0.1948	-12.9449
G_1 dendrimer	303.15	0.9914	0.1238	-6.50650
TCT	303.15	0.9915	0.0298	1.53170
TAT	303.15	0.9912	0.1539	9.26400
THT	303.15	0.9895	1.6611	-87.5732
G_2 dendrimer	298.15	0.9968	0.1947	-12.94490
G_2 dendrimer	303.15	0.9915	0.1238	-6.50650

The B data were used for shape determination using Einstein model[9] from specific viscosities ($\eta_{sp} = (\eta/\eta_0-1)$) with $\eta_{sp} = 2.5$ v/V relation. The v is volume occupied by dendrimer molecule (as spheres) and V is the total volume of the solution in the viscometer bulb. Einstein[31] reported v/V < 2.5 for spherical and v/V > 2.5 for nonspherical molecules. The dendrimers showed v/V < 2.5. The B is noted as intrinsic viscosities [η] and were fitted with Houwink-Sakurada equation[23] for molecular weight determination incorporating restrictions suggested by Frechet, Hawker and Gitsov[20], and Flory and Leutner[8] The experimental viscosities are plotted in Fig. 2.

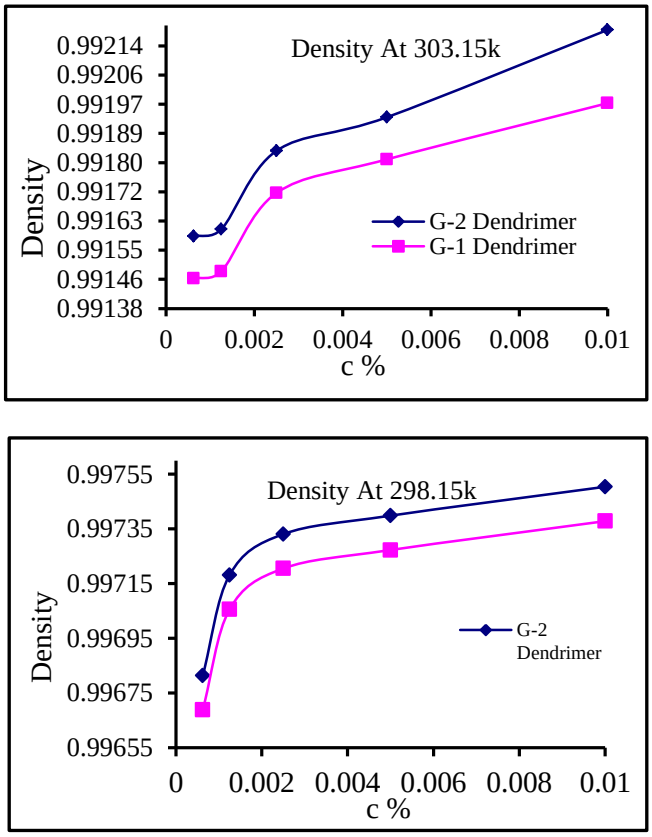

Figure 1: *The densities (ρ) in 10^3kg m^{-3} at 303.15 (a) and at 298.15 K (b) on Y-axis, and concentrations, c, on X-axis, for G_1 and G_2 dendrimers*

Discussion

Limiting density ρ^0

The ρ^0 values are G_1 (298.15)>TCT (303.15)> G_1 (303.15)>TAT (303.15)>THT (303.15 K) (Table 1 and Fig.1). A maximum ρ^0 value is 0.99671x10^3 kg m^{-3} for G_1 (298.15 K) and is minimum value 0.98964x10^3 kg m^{-3} for THT at 303.15 K are noted with stronger cohesive forces of dendrimer due to π conjugation of core ring and six ethyl malonate groups of G_1. Both

the dendrimers developed stronger heteromolecular forces. The G_1 at 303.15 K showed the lesser ρ^0 values than those of the G_1 at 298.15 K. The densities with an increase in temperature by 5ºC from 298.15 to 303.15 K decreased due to an expansion in molar volume. The difference in ρ^0 values is slightly lower with a minimum expansion in volume. The THT with a minimum ρ^0 value inferred weaker intermolecular hydrogen bonding.

The 3-OH groups of the THT developed weaker forces on the interactions than those of a chloride anion of the TCT and acetate group of TAT. It attributed to a lower size of chloride ion (Cl^-) and electronegativity of >C=O group of CH_3COO. The ρ values of the G_1 at 298.15 are higher than that of water but the values at 303.15 K are lower than those at 298.15 K. However the ρ values increased with concentration (Fig.1). The lower values for G_1 at 303.15 K depicted weaker intermolecular forces between TDEMTA and water than those of water-water due to hydrogen bonding. It inferred the G_1 a weaker water structure breaker due to 6 branches

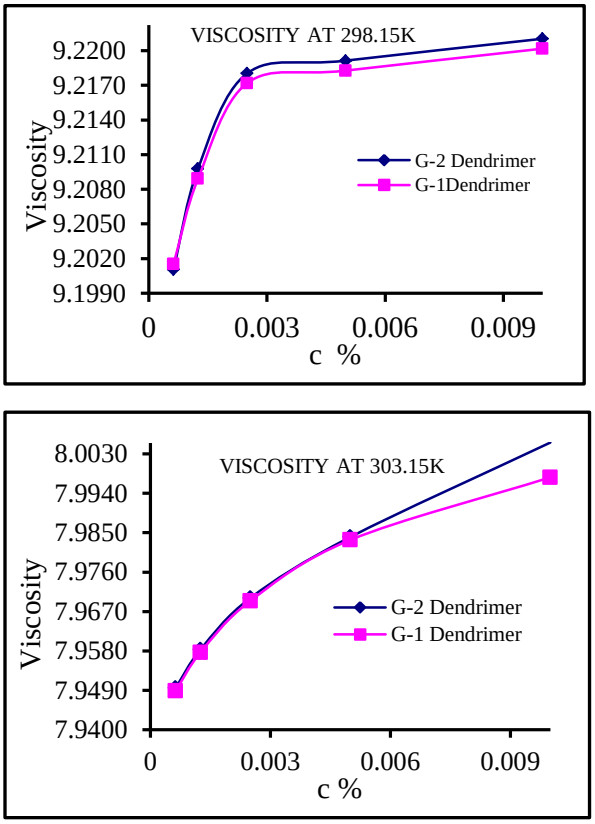

Figure 2: *The viscosities (η) in 10^{-2}kg $m^{-1}s^{-1}$ at 298.15 K (a) and at 303.15 K (b) on Y-axis, and concentrations, c, on X-axis, for the G_1 and G_2 dendrimers.*

terminated by ethyl group of malonate ester. However their trend remains similar for G_2 but the magnitude of an effect is higher. It illustrated integrated dendrimer structure and π conjugations of core which is not so effective for interaction. Perhaps the 6 ethyl groups are responsible for

such behaviour but in case of the G_2, the 12 ethyl groups, due to more branching, an effect is further weakened. However the ρ^0 values of G_1 at 298.15 K are lowered than those of water by 0.34 kg m^{-3} and from the 298.15 to 303.15 K, the values are lowered by 5.31 kg m^{-3}. It illustrates weaker intermolecular forces due to much reorientation in dendrimer structure. Thus at 303.15 K, the ρ^0 values for G_1 are lower by 4.25 kg m^{-3} than those of the water, with higher intermolecular forces with G_1 at 303.15 to 298.15 K.

The S_d values for G_1 are higher at 298.15 to 303.15 K by 70.94 kg^2 m^{-3} mol^{-1}, due to stronger intermolecular interaction with composition. However the TCT, TAT and THT showed lower ρ^0 values than those of the dendrimers at 303.15 K. The THT showed the lowest ρ^0 values with highest S_d value due to stronger intermolecular forces with composition. The S_d values are THT (303.15)>G_1 (298.15)>TAT (303.15)>TCT (303.15 K). Contrary its ρ^0 values, the S_d values (Table 1) are maximum for THT with stronger THT-THT interaction with stronger hydrogen bonding because of 3-OH groups but with TCT and the TCT-TCT interaction are weaker due to chloride. Hence chloride anion developed weakest solute-solute interaction and the TAT with acetate anion also weaker solute-solute interaction than those of the THT. The THT developed stronger solute-solute interactions due to an interrupted π conjugation, although the -OH group showed larger activity but π conjugation caused least effect on TCT for solute-solute interaction. By comparing these values of the G_1 at 298.15 to 303.15 K, the values are lower at 303.15 K, due to weaker temperature effect on solute-solute interaction. Similarly the higher heteromolecular forces with G_2 contrary to G_1 illustrated an effect of an addition of 6 more malonate ester groups to a G_1. Thus the ρ^0 values of G_2 (Table 1) are slightly higher than those of the G_1. However the densities with conc. increased. Slightly higher v/V values for G_2 inferred larger molecular size but due to 2 times more branching with peculiar structure, it enhanced its compatibility with higher densities than those of the G_1. Thereby with tiers, the dendrimers form a denser network, perhaps due to intramolecular and intermolecular hydrogen bonding, with higher densities. This is attributed to a larger number of active sites for hydrogen bonding dubbing the effects and response of lone pair of nitrogen atoms of a core. Like G_1, the ρ^0 values of G_2 with increase in temperature by 5^0C, show slightly lower decrease. It inferred resistance of branching to a molecular expansion due to intra and intermolecular hydrogen bonding with less structural reorientation.

The lower ρ^0 values of G_2 (table 1) at 303.15 K denoted weaker heteromolecular forces between dendrimer and water than those of water-water. Hence the dendrimers with highly branched structures, for example, the 6 branches in the G_1 and 12 in G_2 could not to disrupt the water structure due to stearic hindrance on the C atoms of chains. Thus the water may form a cage around them with slightly stronger hydrophobic interaction.[27] The S_d' data for the G_1 and the G_2 are equal at both the temperatures due to their equal interaction strength with increase in the composition but the markers showed their trends as TAT > TCT > THT with 9.264, 1.5317 and -87.5732 respectively. It inferred that acetate ions developed stronger interactions with increase in its composition the chloride also developed slightly stronger interactions but the OH^- groups were not so effective with respect increase in concentration of the THT molecules.

Viscosities

The viscosity is an arrangement of intermolecular forces to get oriented to flow through a fine capillary with certain activation energy. The dendrimer at 298.15 K has higher viscosities

than that of the water by $0.2505x10^{-4}$ kg $m^{-1}s^{-1}$, which decreased at 303.15 K (Figs. 1 and 2). The G_1 with 6 branches of ethyl malonate and spherical size developed higher Newtonian forces with stronger frictional forces on adjacent layer of their laminar flows. These forces increased many times for G_2 with greater rotational and electronic rearrangement due to greater entropic changes. The viscosities for the G_2 are slightly higher than those of the G_1 with a similar flow dynamics of the G_2 (Figs. 1 and 2). Hence, more branching developed higher hydrodynamic volume. The molecular size is estimated with composition**,** it elucidated structural reorientation. The solvents also contributed to this behaviour, for example, the water is noted as a poor solvent for the macromolecules. Our studies were conducted in aqueous solutions to avoid a statistical size of a coil with chain length.

Conclusion

The densities and viscosities inferred similarity in structures of 1^{st} and 2^{nd} tier dendrimers and are higher for G_2 than those of the G_1. It was noted that the larger numbers of branching developed stronger intra and intermolecular interactions with higher molecular stability. The Borosil Mansingh Survismeter is R4M4 (Reduce Reuse Recycle Redesign Multipurpose Multidimensional Multifaceted Multitracking) model to save resources and infrastructure. The studies could act as effective physicochemical properties indicators (PCI) for protein unfolding, molecular extensions and intensions with molionic designs, extricular molecular frontiers, intricacies, bioremediation of toxic metal or molecules via interstitial reorientations with intrinsic molecular activities displayed through physicochemical properties (PCP). Architectural molecules have intensive PCP acting as PCI where surface tensions, interfacial tension, wetting coefficient, viscosity, friccohesity and activations energy data with encapsulation and entanglement enhance interacting activities.

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