Volumetric and Viscometric Properties of N-Acetylcysteine in Dimethylformamide Containing Binary and Ternary Mixtures

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Dedicated

To

The oppressed people all over the World

Declaration

This is to certify that the thesis work entitled "**Volumetric and Viscometric Properties of N-Acetylcysteine in Dimethylformamide Containing Binary and Ternary Mixtures**" has been carried out by **Gopal Pal** in the Department of Chemistry, Khulna University of Engineering & Technology, Khulna, Bangladesh. The above thesis work or any part of this work has not been submitted anywhere for the award of any degree or diploma.

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Abstract

The density and viscosity of NAC (~0.10 to ~1.00) mol.L^{-1} in H_2O, DMF and DMF–H_2O mixed solutions were measured and studied over the entire molarity range with in the temperature range of 298.15 to 318.15 K at 5 K interval. The apparent molar volumes, φ_v were determined from density values experimented by Density and Sound Velocity Meter (DSA 5000M) Anton Paar, Austria. In the NAC–H_2O and NAC in [1:4] and [2:3] [DMF–H_2O] solvent systems the apparent molar volumes of NAC were found to be increased, whereas in the NAC–DMF and NAC in [4:1] and [3:2] [DMF–H_2O] solvent systems apparent molar volumes of NAC were found to be decreased. Apparent molar volume at infinite dilution, φ_v^0 and S_v values were also computed according to the experimented density values. The apparent molar volume at infinite dilution provided an idea about the presence of solute–solvent interactions of the investigated systems. Sv, the experimental slopes which provided an idea about the prevailing solute–solute interactions in the mixtures. Both φ_v^0 and S_v values indicated that there both solute-solute and solute-solvent interactions present in the binary as well as in ternary solutions.

The investigated systems showed hasty increase of viscosity values with the increased NAC concentration but the values of viscosity decreased with the increase of temperature. In binary and ternary systems showed the similar trend viscosity changes but in different order of magnitude. The order for binary and ternary systems are: NAC–DMF > NAC–H_2O and NAC in [3:2] [DMF–H_2O] > NAC in [4:1] [DMF–H_2O] > NAC in [2:3] [DMF–H_2O] > NAC in [1:4] [DMF–H_2O] > NAC–DMF > NAC–H_2O, respectively. The viscosity values were employed to determine the viscosity coefficients i.e., A and B-coefficients; change of free energy, ΔG^*; change of enthalpy, ΔH^* as well as change of entropy, ΔS^*. Negative values of A and positive values of B co-efficients suggesting that weak solute-solute but strong solute-solvent interaction present in the binary and ternary solution, respectively. From these thermodynamic parameters state of the spontaneity of the investigated systems were known. On the basis of this data, the predominant molecular interactions occurring between NAC–H_2O and NAC in [1:4] and [2:3] [DMF–H_2O] solvent systems were found to be solute-solute interaction, where as in NAC–DMF and NAC in [4:1] and [3:2] [DMF–H_2O] solvent systems solute-solvent interaction were predominant.

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Symbols/ Abbreviations	Explanation
K_d	Dissociation Constant
λ_i	Ionic conductance
η	Viscosity
λ_1^0	Limiting Ionic conductance
A	Area of contact between the two layers
f	Tangential force
ϕ	Fluidity
l	Length
Pa.s	Pascal-Second
cP	centipoise
mPa.s	Milli-Pascal-second
v	Velocity
r	Radius
P	Pressure
t	Flow time
ρ	Density of the liquid/solution
φ_v	Apparent molar volume
φ_v^0	Apparent molar volume at infinite dilution
ΔG^*	Free energy
ΔH^*	Change of Enthalpy
ΔS^*	Change of Entropy
g	Acceleration due to gravity
NAC	N-Acetylcysteine
DMF	Dimethylformamide
IUPAC	The International Union of Pure and Applied Chemistry

CHAPTER I

Introduction

1.1 General

As fundamental and important properties of solution, viscosity and volume could provide a lot of information on the structures and molecular interactions of liquid mixtures. Viscosity and volume are different types of properties of one solution and there is a certain relationship between them. So by measuring and studying them together, relatively more realistic and comprehensive information could be expected to be gained. The relationship between them could also be studied.

Although there are many works on either volume measurements or viscosity measurements of liquid mixtures, there are much fewer investigations on them together. So studies on the relationship between them are scarce. Much more attention to this aspect has been paid here. On this aspect the achievements were first made by Singh p. p. [1] and Singh *et al.* [2]. Relatively, viscometric properties could provide more and deeper information on molecular interactions.

1.2 The phenomena of solute-solvent interaction

Revelation of the nature of ion-solvent interaction [3–4] and interpretation of the thermodynamic and transport processes in terms of such parameters as effective size of the solvated ions in solutions have been two of the most difficult problems in the understanding of electrolytic solutions. This is because there is not satisfactory model to represent the various phenomena that occur in solution and the incompleteness in the understanding of the structure of the liquids in general. There are a number of evidences of solvation of ions [3–4] or solute molecules a number of studies have discussed the effect of solvation on the equilibrium properties of liquids.

The process of solvation and the process of dissolution are known to be closely related. When ionic crystal is added to a solvent, the electrostatic force of attraction between the oppositely charged ions in the crystal have to overcome by interposing solvent layers around each of the ions. The ability of a solvent to dissolve a crystal is reflected by the following properties, its dielectric properties, polarity, degree of self-association and its ability to solvate. Studies on the phenomena of solvation have led to the conclusions that:

(i) The ionic compounds are moderately soluble in dipolar aprotic solvents of relatively high dielectric constant but are much more soluble in water and other hydroxylic solvents like methanol. A number of inorganic salts are dissociated in acetonitrile, which is otherwise known to solvate cations and anions rather poorly [5].

(ii) The dielectric constant alone is not an adequate measure of solvating ability and may even play a major role in determining the solvation of ionic species. Cations should be better solvated in solvents having atoms with an unshared electron pair like nitrogen and oxygen. The cations have been found to be strongly solvated in highly polar solvents with the negative charge localized on an oxygen atom, e.g. in sulphur dioxide, dimethylsulfoxide, phosphorus oxide, dimethylformamide [6]. Potassium iodide is less soluble than sodium iodide in methanol or water [7], but in dimethylsulfoxide or DMF the reverse is true, which could be due to differences of cation solvation.

The anions have been found to be solvated in two ways:

(i) Small ions are mostly solvated by hydrogen bonding which is superimposed upon solvation by ion-dipole interactions, and

(ii) Large ions are solvated by interaction due to mutual polarizability of the anions and the solvent superimposed upon solvation by dipole interactions. Thus while the anions are more strongly solvated in hydrogen bonding solvents than in dipolar aprotic solvents, the cations are better solvated in the latter type of solvents.

The solubility of halides in various solvents generally follows the order:

Iodides > bromides > chlorides > fluorides

The alkaline halides are more soluble in hydroxylic solvents than in the dipolar aprotic solvents like acetonitrile and acetone. These are found to be more soluble in acetonitrile than in acetone [8]. Electrolytes may be divided into two categories: ionophores and ionogens. While the former are ionic in character in the crystalline state as well as in the fused state and in highly dilute solutions, the latter have molecular crystal lattice and ionize in solution only if suitable interaction occurs with the solvent molecules.

The ionophores may exist in solution as an equilibrium mixture containing ion-pairs and free ions [9].

$$M^+X^- \rightleftharpoons \underset{\text{Solvated}}{M^+} + \underset{\text{Solvated}}{X^-}$$

The ion-pairs are of oppositely charged ions having life terms sufficiently long to be recognized as kinetic entities in solution and in which only electrostatic forces are assumed [3]. Fuoss *et al*. [10] have studied intensely the dependence of the dissociation constant, K_d, on the dielectric constant, the temperature and the nature of the salt. It was found to be large for solvents having high dielectric constant. It has also been found to be dependent on the distance of closest approach of the ions in the ion pairs. For hydroxylic solvents, large ions have larger K_d values and lower conductance values than smaller ions, which doesn't hold for other solvents.

Interaction of the ions with the solvent molecules causes low conductance. Na^+ ion behaves as a large ion as the K_d of iodides of Bu_4N^+ and Na^+ are found to be of the same order. Small ions like Li^+, F^- have low conductance in acetone [11] but have low K_d values which have been attributed to the loss of the solvent molecules from the ion-pairs [11]. Solute-solvent interactions have been studied in details by various methods; some important ones may be listed as follows:

(i) Study of the solute-solvent interactions through transference experiments.

(ii) The effect of solvation on the ionic conductance.

(iii) The experiments applying stoke’s law and their relevance to the nature of solvation.

(iv) Polarographic measurements of solutions.

(v) The spectral results due to the presence of the ions in solutions.

A relationship between the values of the limiting equivalent ionic conductance, λ_i and the viscosity, η value was advocated and utilized by Walden and others to study the solute-solvent interactions [12]. In one approach which assumes the constancy of the product $\lambda_i\eta$ the effects of variation of temperature, viscosity and variation of the solvent were studied. For large organic ions [12], the temperature co-efficient was found to be nearly constant in water as well as other non-aqueous solvents, while for the other ions it showed variations. For changing solvents, the product was found to vary widely in the case of inorganic ions which have been interpreted to be due to differences in solvation numbers of the ion in the various solvents. In another approach to this study Pure and Sherrington [13] used the relation between viscosity η_t, and limiting ionic conductance λ_i^0, to measure the radii of interaction of solvent and solute, called stoke's law radii, r. They compared the crystallographic radii of some cations and anions with stoke's law radii in the case of dimethylamide and dimethylsulphoxide solvents. They found the degree of solvation to decrease from lithium to cesium and to be less for silver and ammonium ions which have nearly comparable crystallographic radii. They postulated the anions to be unsolvated in dipolar aprotic solvents as the radii obtained are of the same order as that of the crystallographic radii, and that the negative end of the dipole in the solvent molecule is unshielded while the positive end is protected by two methyl groups, so that the cations, but not the anions are solvated by these solvents. Volumetric and viscometric measurement provides valuable tool for the determination of interaction among solutes and solvents.

1.3 Viscosity

Viscosity means viscous ability. Simply, viscosity of a material is resistance to flow. The internal friction which opposes the relative motion of the adjacent layers of a fluid causes for the resistance to flow. When a fluid is flowing through a cylindrical tube, this internal friction arises because of intermolecular friction. Molecules are a slower moving layer try to decrease the velocity of the molecules in a faster moving layer and vice versa.

Viscosity is really a frictional effect experienced by one layer of a liquid in moving past another in much the same way as an object experiences frictional resistance when dragged on a surface. The friction force, *f*, resisting the flow of one layer of fluid past the adjacent layer is proportional to the area, A, of the interface between the layers and to $\frac{du}{dr}$, the velocity gradient. This is Newton’s law and is given by

$$f = \eta A \frac{du}{dr}$$

Where η (eta, a Greek letter), the constant of proportionality, is called the co-efficient of viscosity. When the velocity gradient is unity and the area is 1 sq.cm, η is equal to the force; or the co-efficient of viscosity,η may be defined as the force per 1 sq.cm required to maintain a difference of velocity of 1 cm per second between two parallel layers 1 cm apart. The reciprocal of the co-efficient of viscosity is known as the fluidity, $\varnothing$, or $\varnothing = \frac{1}{\eta}$

Fluidity is a measure of the ease with which a liquid can flow. The connection between these quantities was first derived by J. L. M. Poiseuille in 1844, known as the Poiseuille's equation [14]. If aliquid with a coefficient of viscosity (η) flows with a uniform velocity, at a rate of v cm^3 in t seconds through a narrow tube of radius r cm, and length 1 cm under a driving pressure of P dynes cm^{-2} then [14]:

$$\eta = \frac{\pi P r^4 t}{8 l v} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1.1.1)$$

This equation known as Poiseuille equation holds accurately for stream-line flow but not for the turbulent flow which sets as higher velocities.

Where, η is a proportionality constant, known as the coefficient of viscosity or simply viscosity of the liquid. The CGS unit of viscosity i.e., dynes sec cm^{-2} = g $cm^{-1}sec^{-1}$ is called poise, in honor of J. L. M. Poiseuille who is the pioneer in the study of viscosity. The SI unit of viscosity is the Pascal-second (Pa.s). Since viscosity of liquid is usually very small, it is usually expressed in millipoise (mP) or centipoise (cP) or mPa.s.

1.3.1 Factors affecting viscosity

Viscosity is first and foremost function of material. Most ordinary liquids have viscosities on the order of 1 to 1000 mPa.s, while gases have viscosities on the order of 1 to 10 µPa.s. Pastes, gels, emulsions, and other complex liquids are harder to summarize. Some fats like butter or margarine are so viscous that they seem more like soft solids than like flowing liquids.

Temperature: The viscosity of a simple liquid decreases with increasing temperature (and vice versa). As temperature increases, the average speed of the molecules in a liquid increases and the amount of time they spend "in contact" with their nearest neighbors decreases. Thus, as temperature increases, the average intermolecular forces decrease.

The exact manner in which the two quantities vary is nonlinear and changes abruptly when the liquid changes phase.

Pressure: Viscosity is normally independent of pressure, but liquids under extreme pressure often experience an increase in viscosity. Since liquids are normally incompressible, an increase in pressure doesn't really bring the molecules significantly closer together. Simple models of molecular interactions won't work to explain this behavior and, to my knowledge, there is no generally accepted more complex model that does. The liquid phase is probably the least well understood of all the phases of matte
While liquids get runnier as they get hotter, gases get thicker. The viscosity of gases increases as temperature increases and is approximately proportional to the square root of temperature. This is due to the increase in the frequency of intermolecular collisions at higher temperatures. Since most of the time the molecules in a gas are flying freely through the void, anything that increases the number of times one molecule is in contact with another will decrease the ability of the molecules as a whole to engage in the coordinated movement. The more these molecules collide with one another, the more disorganized their motion becomes.

Cohesive forces: Cohesive forces are the intermolecular forces (such as those from hydrogen bonding and van der Waals forces) which cause a tendency in liquids to resist separation. These attractive forces exist between molecules of the same substance. For instance, rain falls in droplets, rather than a fine mist, because water has strong cohesion which pulls its molecules tightly together, forming droplets. This force tends to unite molecules of a liquid, gathering them into relatively large clusters due to the molecules' dislike for its surrounding. The materials having stronger cohesive forces normally exhibit lower viscosities and vice-versa.

Adhesive force: Adhesive forces are the attractive forces between unlike molecules. They are caused by forces acting between two substances, such as mechanical forces (sticking together) and electrostatic forces (attraction due to opposing charges). In the case of a liquid wetting agent, adhesion causes the liquid to cling to the surface on which it rests. When water is poured on clean glass, it tends to spread, forming a thin, uniform film over the glasses surface. This is because the adhesive forces between water and glass are strong enough to pull the water molecules out of their spherical formation and hold them against the surface of the glass, thus avoiding the repulsion between like molecules. The materials having stronger adhesive forces normally reveal higher viscosities and vice-versa.

1.4 Properties of Dimethylformamide

Dimethylformamide is an organic compound with the formula $(CH_3)_2NC(O)H$. It is colorless liquid miscible with water and the majority of organic liquids. DMF is a common solvent for chemical reactions. Density of DMF is 0.95 g cm^{-3} at 20 °C similar to that of water. DMF is well-known material that is used as selective solvents in extraction or extractive distillation processes**.** N,N' -Dimethylformamide (DMF) has a large dipole moment and a high dielectric constant [15]; therefore, it may work as an aprotic protophilic solvent used in the synthesis of pharmaceuticals, in agricultural chemistry, and as a solvent for polymers [16]. It is used to a great extent as substitutes for traditional organic solvents in electrochemistry, chemical reactions, catalysis, separations, heat transfer, lubrication, and analysis. Some of its benefits, as solvents, are its high thermal stability, excellent dissolution properties for most organic and inorganic compounds, and non-flammability [17−18].

DMF is an important industrial liquid that has found various applications in different areas [19]. It is an interesting molecule, hydrophobic methyl groups can disturb the water structure. Besides, “cross” hydrogen bonds are expected to form between molecules belonging to two different species. Computer modelling studies can be classified according to the details of the force fields describing the internal structure of the DMF molecule. Specifically, one set of models with either five or six force centers (in each of models the methyl group has been considered as a single site) was explored in [20–23]. The primary use of DMF is as a solvent with low evaporation rate. DMF is used in the production of acrylic fiber sand plastics. It is also used as a solvent in peptide coupling for pharmaceuticals, in the development and production of pesticides, and in the manufacture of adhesives, synthetic leathers, fibers, films, and surface coatings [24]. DMF is effective at separating and suspending carbon nanotubes, and is recommended by the NIST for use in near infrared spectroscopy of such [25].

Table 1.1:Some properties of Dimethylformamide

Property	Data
Chemical Name	Dimethylformamide
Chemical formula	$(CH_3)_2$ NC(O)H
Appearance	Colorless liquid
Molecular mass	73.095 g·mol^{-1}
Melting point	−60.5 °C
Boiling point	152 to 154 °C
Density	0.948 g mL^{-1}
Viscosity	0.92 mPa.S (at 20 °C)
Dipole moment	3.86 D
Solubility	Soluble in water

1.5 Properties of Water

Water has a very simple atomic structure. The nature of the atomic structure of water causes its molecules to have unique electrochemical properties. The hydrogen side of the water molecule has a slight positive charge. On the other side of the molecule a negative charge exists. This molecular polarity causes water to be a powerful solvent and is responsible for its strong surface tension.

When the water molecule makes a physical phase change its molecules arrange themselves in distinctly different patterns. The molecular arrangement taken by ice (the solid form of the water molecule) leads to an increase in volume and a decrease in density. Expansion of the water molecule at freezing allows ice to float on top of liquid water.

1.5.1 Structure of water

It has been recognized that water is an ‘anomalous’ liquid many of its properties is differ essentially from normal liquids of simple structures [26]. The deviations from regularity indicate some kind of association of water molecules. The notable unique physical properties exhibited by liquid water are [27] : i) negative volume of melting ii) density maximum in normal liquid range (at 4^0C) iii) isothermal compressibility minimum in the normal liquid range at (46^0C) iv) numerous crystalline polymorphs v) high dielectric constant vi) abnormally high melting, boiling and critical temperatures for such a low molecular weight substance that is neither ionic nor metallic vii) increasing liquid fluidity with increasing pressure and viii) high mobility transport for $H^+$and OH^- ions pure water has a unique molecular structure. The O-H bond length is 0.096 nm and the H-O-H angle 104.5^0. For a very long time the physical and the chemists have pondered over the possible structural arrangements that may be responsible for imparting very unusual properties to water. To understand the solute water interaction the most fundamental problem in solution chemistry the knowledge of water structure is a prerequisite. The physico-chemical properties of aqueous solution in most of the cares are interpreted in terms of the structural change produced by solute molecules. It is recognized that an understating of the structural changes in the solvent may be crucial to study of the role of water in biological systems. Various structural models that have been developed to describe the properties of water may generally be grouped into two categories, namely the continuum model and the mixture models. The continuum models [28, 29] treat liquid water as a uniform dielectric medium, and when averaged over a large number of molecules the environment about a particular molecules is considered to be the same as about any other molecules that is the behavior of all the molecules is equivalent. The mixture model theories [30, 31 and 32] depict the water as being a mixture of short lived liquid clusters of varying extents consisting of highly hydrogen bonded molecules which are mixed with and which alternates role with non-bonded monomers. Among the mixture models, the flickering cluster of Frank and Wen [33], later developed by Nemethy and Scherage [28], is commonly adopted in solution chemistry. Properties of dilute aqueous solutions in terms of structural changes brought about by the solutes can be explained more satisfactorily using this model than any other model. According to this model the tetrahedraly hydrogen bonded clusters, referred to as bulky water $(H_2O)_A$, are in dynamic equilibrium with the monomers, referred to as dense water, $(H_2O)_B$ as represented by [30].

$$(H_2O)_A \rightleftharpoons (H_2O)_B$$

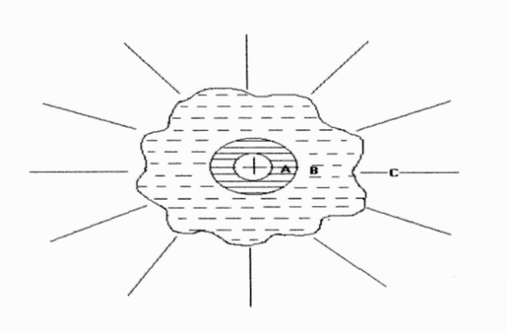


Figure 1.1: Frank and Wen model for the structure modification produce by an ion

The hydrogen bonding in the clusters is postulated [34] to be cooperative phenomenon. So when one bond forms several other also come into existence will be dissolved. The properties of solution can be accounted for in terms of solvent-solvent, solvent-solute and solute-solute interaction. In terms of thermodynamics, the concentration dependence of a given property extrapolated to the limit of infinite dilution provides a measure of solute-solvent interactions. Solute-water interaction or hydration phenomenon can be conveniently classified into three basic types:

i. Hydrophilic Hydration
ii. Ionic hydration
iii. Hydrophobic hydration

The introduction of a solute into liquid water produces changes in the properties of the solvent which are analogous to these brought about by temperature or pressure. The solute that shifts the equilibrium to the left and increase the average half-life of the clusters is termed as structure maker whereas that which has an effect in the opposite direction is called 'Structure breaker. The experimental result on various macroscopic properties provides useful information for proper understanding of specific interactions between the components and the structure of the solution. The thermodynamic and transport properties are sensitive to the solute-solvent, solute-solute, and solvent-solvent interaction. In solution systems these three types of interaction are possible but solute-solute interaction are negligible at dilute solutions. The concentration dependencies of the thermodynamic properties are a measure of solute-solute interaction and in the limit of infinite dilutions these parameters serve as a measure of solute-solvent interactions.

The solute induced changes in water structure also result in a change in solution viscosity.

1.5.2 Hydrophilic hydration

Solvation occurs as the consequences of solute-solvent interactions different from those between solvent molecules themselves. The solubilization of a solute molecule in water is characterized by changes in the water structure that depend on the nature of the solute. Dissolution of any solute will disrupt the arrangement of water molecules in the liquid state and create a hydration shell around the solute molecule. If the solute is an ionic species, then this hydration shell is characterized to extend from an inner layer where water molecules near the charge species are strongly polarized and oriented by the electrostatic field, through an intermediate region where water molecules are significantly polarized but not strongly oriented, to an outer solvent region of bulk water where the water molecules are only slightly polarized by the electric field of the ion [35].

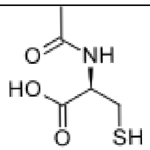
1.5.3 Hydrophobic hydration

The hydrophobic effect refers to the combined phenomena of low solubility and the entropy dominated character of the solvation energy of non-polar substances in aqueous media [36]. It is also reflected by anomalous behavior in other thermodynamic properties, such as the partial molar enthalpies, heat capacities, and volumes of the nonpolar solutes in water. This effect originated from as much stronger attractive interaction energy between the nonpolar solutes merged in water than their van der Waals interaction in free space [37]. The tendency of relativity nonpolar molecules to “stick together” in aqueous solution is denoted as the hydrophobic interaction [38]. It results from hydrophobic hydration of a nonpolar molecule. Because hydrophobic hydration plays an important role in facilitating amphiphiles to aggregates in the aqueous bulk phase and to absorb, excessively, at the aqueous solution/air interface, it has been an ongoing objective of chemists working in these areas to seek a clear understanding of the molecular nature behind the subtle hydration phenomenon occurring between nonpolar solutes and water. A brief but detailed account of the general aspects of hydrophobic hydration, which is essential to the rationalization of the results obtained in this work, is given at this point.

1.6 Properties of N-Acetylcysteine

N-Acetyl-L-Cysteine (NAC), the preacetylysed form of simple amino acid cysteine, a synthetic precursor of cysteine and reduced glutathione has been in clinical use for more than 40 years. It is a powerful intracellular antioxidant, antitoxin improves immunity. NAC is a thiol compound which is also called Acetylcysteine, is an amino acid with the molecular formula $C_5H_9NO_3S$, Molar mass of acid 163.195 g/mole .The melting point and boiling point of NAC are 106 °C and 407.7 °C respectively. It is a white crystalline powder with a slightly acidic odor and characteristic sour tasting. It is a solid at room temperature, but dissolutes easily with water, 4ml ALC; practically insoluble in chloroform and ether. The vapor pressure of NAC is estimated 1.1×10^{-5} mm Hg at 25 °C and stable of Stable in ordinary light; stable at temperature up to 120 °C; non-hygroscopic (oxidizes in moist air). The pH of NAC is 2 to 2.75 (1 in 100 ml) and dissociation constants pKa=3.24 (carboxylic acid moiety) and Spectral Properties is Specific optical rotation: +5 °C at 20 °C (concentration = 3 g/100 mL). NAC is not found naturally in food sources; however cysteine is present in most high protein foods. NAC converts into cysteine.

Table 1.2: Some properties of N-Acetylcysteine

Property	Data
Chemical Name	N-Acetylcysteine
Chemical formula	$C_5H_9NO_3S$
Chemical structure	
Appearance	white crystalline powder
Molecular mass	163.195 g/mole

Melting point	109 to 110 °C
Boiling point	407.7 °C at 760 mmHg
pH	2 to 2.75 (1 in 100 ml)
Density	1.294 g/cm^3
Flash Point	200.4 °C

Cysteine is a nonessential amino acid produced by the body. Cysteine is primarily found in animal protein, along with the other ten essential amino acids. Meats such as pork, chicken, sausage, turkey and duck all contain the amino acid cysteine. Fish and lunch meats also contain cysteine. Dairy sources of cysteine include ricotta cheese, cottage cheese, yogurt and eggs. Cysteine can be found in some plant sources plant sources for vegetarians and vegans. Cysteine is found in granola and oat flakes. Vegetables like broccoli, red pepper and onion are significant sources of cysteine. Other plant sources include bananas, garlic, soy beans, linseed and wheat germ. Cysteine is important amino acid, but deficiency is relatively rare. Low levels of cysteine can cause slow growth in children and lowered immunity. Muscle loss, weakness, apathy and liver damage may also be a result of low cysteine in the diet.

NAC is a therapeutic medicine frequently used as a mucolytic agent and for treating acetaminophen hepatotoxicity. It increases the cell reserves of free radicals and acts as an antioxidant. It also inhibits the replication of HIV and prevents apoptosis in neurons. NAC prevents endotoxin-induced degeneration of oligodendrocyte progenitors and hypomyelination in developing rat brain. NAC may have a direct chelating effect on lead as seen by lowered serum lead levels. It prevents lead toxicity and reduces oxidative sequel of lead exposure. NAC crosses cell membranes and is rapidly consumed in producing intracellular glutathione. By reducing extracellular cysteine to cysteine, it acts as a source of SH groups and it can stimulate glutathione synthesis enhance glutathione-S-transferase activity promote detoxification and act directly on reactive oxidant radicals. NAC corrects the reduction in glutathione concentration and results in significant preservation of fluidity of membranes and of the activities of catalase, mitochondrial superoxide dismutase and different forms of glutathione peroxidase in biliary obstructed rats. NAC is a powerful scavenger of hypochlorous acid and is capable of reducing hydroxyl radicals and hydrogen peroxide. SH groups are essential for defense against reactive oxygen species. NAC can also prevent apoptosis caused by oxidative stress and promote cell survival by activating signal regulating pathways. Recently volumetric and viscometric study of N-acetylcysteine in ethanol and ethanol-water systems were performed [39]. From the results it was seen that NAC showed more interaction in ethanol-water mixture than those for individual solvents. So this research is devoted to solution properties of NAC which may have enormous medicinal and biological applications. The solution behavior of NAC has been investigated in versatile solvent, water and common organic solvent dimethylformamide. The investigation has also been carried out in water + dimethylformamide mixed solvents and to the best of my knowledge that hadn’t been done before.

Theoretical Background

1.7 Physical Properties and chemical constitutions

In interpreting the composition, the structure of molecules and the molecular interaction in the binary and ternary systems, it is inevitable to find out the size and the shape of the molecules and the geometry of the arrangement of their constituent atoms. For this purpose the important parameters are bond lengths or interatomic distance and bond angles. The type of atomic and other motions as well as the distribution of electrons around the nuclei must also be ascertained; even for a diatomic molecule a theoretical approach for such information would be complicated. However, the chemical analysis and molecular mass determination would reveal the composition of the molecules, and the study of its chemical properties would unable one to ascertain the group or sequence of atoms in a molecule. But this cannot help us to find out the structures of molecules, as bond length, bond angles, internal atomic and molecular motions, polarity etc. cannot be ascertained precisely.

For such information it is indispensable to study the typical physical properties, such as absorption or emission of radiations, refractivity, light scattering, electrical polarization, magnetic susceptibility, optical rotations etc. The measurement of bulk properties like, density, surface tension, viscosity etc. are also have gained increased importance during the recent years, because not only of their great usefulness in elucidating the composition and structure of molecules, but also the molecular interaction in binary and ternary systems. The various physical properties based upon the measurement of density, viscosity, surface tension, refractive index, dielectric constant etc., have been found to fall into the following four categories [40].

(i) Purely additive properties: An additive property is one, which for a given system, is the sum of the corresponding properties of the constituents. The only strictly additive property is mass, for the mass of a molecule is exactly equal to the sum of the masses of its constituent atoms, and similarly the mass of a mixture is the sum of the separate masses of the constituent parts. There are other molecular properties like molar volume, radioactivity etc. are large additive in nature.

(ii) Purely constitutive properties: The property, which depends entirely upon the arrangement of the atoms in the molecule and not on their number is said to be a purely constitutive property. For example, the optical activity is the property of the asymmetry of the molecule and occurs in all compounds having an overall asymmetry.

(iii) Constitutive and additive properties: These are additive properties, but the additive character is modified by the way in which the atom or constituent parts of a system are linked together. Thus, atomic volume of oxygen in hydroxyl group (–OH) is 7.8 while in ketonic group (=CO) it is 12.2. The molar refraction, molecular viscosity etc. are the other examples of this type.

(iv) Colligative properties: A colligative property is one which depends primarily on the number of molecules concerned and not on their nature and magnitude. These properties are chiefly encountered in the study of dilute solutions. Lowering of vapor pressure, elevation of boiling point, depression of freezing point and osmotic pressure of dilute solutions on the addition of non-volatile solute molecules are such properties.

1.8 Molarity

Molarity, (C) is defined as the number of moles of solute per liter of solution. If n is number of moles of solute and V liters is the volume of the solution then,

$$Molarity(C) = \frac{Number\ of\ moles\ of\ solute}{Volumeofsolution}$$

$$or, C = \frac{n}{V} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.1)$$

The unit of molarity is mol/L

1.9 Molar volume of Mixtures

The volume in mL occupied by 1 mole of any substance is called the molar volume. On the other hand, if ρ is the density and M be the molar mass, molality (m) of a solution is defined as the number of moles of the solute per 1000 g of solvent. Mathematically,

$$Molality\ (\mathrm{m}) = \frac{\text{Number of moles of solute}}{\text{Weight of solvent in gram}} \times 1000$$

$$\text{or,}\ \ \mathrm{m} = \frac{\frac{\mathrm{a}}{\mathrm{M}_2} \times 1000}{\text{Volume of solvent in mL.} \times \text{density of solvent in g cm}^{-3}}$$

$$\text{or, } \mathrm{m} = \frac{\mathrm{a}}{\mathrm{M}_2} \times \frac{1000}{\mathrm{V}_1 \times \rho_0} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.2)$$

Where, a = weight of solute in gram.

M_2 = molecular weight of solute in gram.

V_1 = volume of solvent in mL

ρ_0 = density of solvent in g/cm^3

Specific volume, (V) = $\frac{1}{\rho}$ mLg^{-1} $\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$ (1.2.3)

Molar volume, (V_m) = $\frac{M}{\rho}\, m\, Lmol^{-1} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots$ (1.2.4)

When two components are mixed together, there may be either a positive or a negative deviation in volume. One of cause of positive deviation in volume i.e. volume expansion has been explained by the disruption of the mode of association through H–bonding of liquids. The negative deviation in molar volume i.e. volume contraction has been thought of by many observers, as arising from the

I. compound formation through association
II. decrease in the intermolecular distance between the interacting molecules
III. interstitial accommodation of smaller species in the structural network of the larger species and
IV. change in the bulk structure of either of the substance forming the mixture.

1.10 Apparent molar volume

The apparent molar volume of a solute in solution, generally denoted by φ_v [41]

$$\varphi_v = \frac{V - n_1\overline{V}_1^0}{n_2} \quad \ldots\ldots (1.2.5)$$

Where, V is the volume of solution containing n_1 moles of solvent and n_2 moles of solute and $\overline{V}_1^0$ is the molar volume of the pure solvent at specified temperature and pressure. For binary solution, the apparent molar volume φ_v of an electrolyte in an aqueous solution is given by [42],

$$\varphi_v = \frac{1}{n_2}\left[\frac{n_1M_1 + n_2M_2}{\rho} - n_1\overline{V}_1^0\right] \quad \ldots\ldots (1.2.6)$$

Where, $V = \frac{n_1M_1 + n_2M_2}{\rho}$ and

n_1 and n_2 are the number of moles, M_1 and M_2 are molar masses of the solvent and solute respectively and ρ is the density of the solution. For molar concentration, $n_2 = m$, the molality and n_1, the number of moles of solvent in 1000 g of solvent, the equation for apparent molar volume takes the form [42,43],

$$\varphi_v = \frac{1}{m}\left[\frac{1000 + mM_2}{\rho} - \frac{1000}{\rho_0}\right]$$

$$\text{or, } \varphi_v = \left[\frac{M_2}{\rho} - \frac{1000(\rho - \rho_0)}{m\rho\rho_0}\right] \quad \ldots\ldots (1.2.7)$$

where, ρ_o and ρ are the densities of the solvent and solution.

If the concentration is expressed in molarity (C), the equation (1.2.7) takes the form [44]:

$$\varphi_v = \left[\frac{M_2}{\rho_0} - \frac{1000(\rho - \rho_0)}{C\rho_0}\right] \quad \ldots\ldots (1.2.8)$$

Where, the relation,

$C = \frac{m.\varphi_v.1000}{1000 + \varphi_v.m.\rho_0}$ is used for inter conversion of the concentration in the two scales [37]. The partial molar property of a solute is defined as the change in property when one mole of the solute is added to an infinite amount of solvent, at constant temperature and pressure, so that the concentration of the solution remains virtually unaltered. If 'Y' represents partial molar property of a binary solution at constant temperature and pressure, Y will then be a function of two independent variables n_1 and n_2, which represent the number of moles of the two components present. The partial molar property of component one is then defined by the relation:

$$\overline{Y_1} = \left(\frac{\delta Y}{\delta n_1}\right)_{n_2,P,T} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.9)$$

Similarly for component 2,

$$\overline{Y_2} = \left(\frac{\delta Y}{\delta n_2}\right)_{n_1,P,T} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.10)$$

The partial molar property is designated by a bar above the letter representing the property and by a subscript, which indicates the components to which the value refers. The usefulness of the concept of partial molar property lies in the fact that it may be shown mathematically as,

$$Y_{(n_1,n_2)} = n_1\overline{Y_1} + n_2\overline{Y_2} \text{ at constant T and P} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.11)$$

In respect of the volume of solution, equation 1.2.4 gives directly

$$V = n_1\overline{V_1} + n_2\overline{V_2} \text{ at constant T and P} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.12)$$

At infinite dilution, (m or c →0), the partial molar volume and the apparent molar volume are identical. To obtain reliable φ_v values, it is necessary to measure the density, ρ with great precision because errors in ρ contribute considerably to the uncertainties in φ_v.

The concentration dependence of the apparent molar volume of electrolytes have been described by the Masson equation [45], the Redlich-Mayer equation [47] and Owen-Brinkley equation [46]. Masson [45] found that the apparent molar volume of the electrolytes vary with the square root of the molar concentration as,

$$\varphi_v = \varphi_v^0 + S_v\sqrt{c} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.13)$$

Where, S_v is the experimental slope depending on the nature of the electrolyte.

Redlich and Rosenfeld [40] predicated that a constant limiting law slope S_v, should be obtained for a given electrolyte charge type if the Debye-Huckel limiting law is obeyed.

By differentiating the Debye-Huckel limiting law for activity coefficients with respect to pressure, the theoretical limiting law slope S_v, could be calculated using the equation,

$$S_v = KW^{3/2} \cdots\cdots (1.2.14)$$

Where, the terms K and W are given by

$$K = N^2 e^3 \left(\frac{8\pi}{100D^3RT} \right)^{1/2} \left\{ \left(\frac{\delta \ln D}{\delta \rho} \right) - \left(\frac{\beta}{3} \right) \right\} \cdots\cdots (1.2.15)$$

And, $W = 0.5 \sum \gamma_i Z_i^2 \cdots\cdots (1.2.16)$

where, β is the compressibility of the solvent, γ_i is the number of ions of the species i of valency Z_i formed by one molecule of the electrolyte and the other symbols have their usual significance [47]. For dilute solutions the limiting law for the concentration dependence of the apparent molar volume of electrolytes is given by the equation,

$\varphi_v = \varphi_v^0 + KW^{3/2}\sqrt{C} \cdots\cdots (1.2.17)$and for not too low concentrations, the concentration dependence can be represented as,

$$\varphi_v = \varphi_v^0 + S_v\sqrt{C} + b_v C \cdots\cdots (1.2.18)$$

Where, S_v is the theoretical limiting law slope and b_v an empirical constant.

1.11 Viscosity

Viscosity means viscous ability. The internal friction opposes the relative motion of adjacent layers of a fluid. When a fluid is flowing through a cylindrical tube, layers just touching the sides of the tubes are stationary and velocities of the adjacent layers increases towards the center of the tube, the layer in the center of the tube having the maximum velocity. There thus exists a velocity gradient. Molecules are a slower moving layer try to decrease the velocity of the molecules in a faster moving layer and vice versa, with a result that some tangential force is required to maintain uniform flow. This tangential force will depend upon two factors,

(i) Area of contact ‘A’ between the two layers and

(ii) Velocity gradient $\frac{dv}{dx}$

Thus, $f \propto A \frac{dv}{dx}$

Or $$f = \eta A \frac{dv}{dx} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.2.20)$$

Where, η is a proportionality constant, known as the coefficient of viscosity or simply viscosity of the liquid. Thus, the coefficient of viscosity may be defined as the force per unit area required to maintain unit difference in velocity between two parallel layers of liquid unit distance apart.

The reciprocal of viscosity called the fluidity (ϕ) is given by the relation.

$$\phi = \frac{1}{\eta} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.2.21)$$

If a liquid with a coefficient of viscosity (η) flows with a uniform velocity, at a rate of V cm^3 in t seconds through a narrow tube of radius r cm, and length 1 cm under a driving pressure of p dynes cm^{-2} then according to J.L.M. Poiseuille [48]:

$$\eta = \frac{\pi P r^4 t}{8 l v} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.2.22)$$

This equation known as Poiseuille's holds accurately for stream-line flow but not for the turbulent flow which sets as higher velocities. After correction for kinetic energy, the equation becomes,

$$\eta = \frac{\pi P r^4 t}{8 l v} - \frac{\rho V}{8 \pi l t} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.2.23)$$

Where, ρ represents the density of the liquid/solution. However, in practical purposes, the correction factor is generally ignored.

The driving pressure $P = h\rho g$, where h is the difference in height of the surface of the two reservoirs, since the external pressure is the same at the surface of both reservoirs, g = acceleration due to gravity and ρ= the density of liquid. Thus the equation (1.2.22) becomes,

$$\eta = \frac{\pi h \rho g r^4 t}{8 v l} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.2.24)$$

For a particular viscometer h, l, r and v are fixed, so the equation (1.2.24) becomes,

$$\eta = A \rho t \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.2.25)$$

where, $A = \frac{\pi h g r^4}{8 v l}$; called the calibration constant of the viscometer used.

Putting the values of A, ρ and *to* f the investigated liquid in equation (1.2.25), the coefficient of viscosity can be obtained for a liquid at a definite temperature.

The CGS Unit of viscosity is poise, in honor of J.L.M. Poiseuille. The SI unit of viscosity is the pascal-second (Pa·s). Since viscosity of liquid is usually very small, it is usually expressed in centipoise (cP) or mPa.s.

1.12 Viscosity and temperature

The viscosity of a liquid generally decreases with the increase of temperature. Evaluation of energy of activation for viscous flow can be stated by the Arrhenius equation as follows:

$$\eta = Ae^{-\epsilon_a/RT} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.26)$$

Where, A is Arrhenius constant and ε is energy of activation for viscous flow. The linear form of the equation 1.2.26 is as follows:

$$\ln\eta = \ln A - \frac{\epsilon_a}{RT} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.27)$$

$\ln\eta$against$\frac{1}{T}$ offer straight line. From the slope and intercept the energy of activationand Arrhenius constant can be determined.

1.13 Different thermodynamic parameters

Eyring and co-workers [49] using absolute reaction rate theory and partition functions corrected viscosity, η as follows:

$$\eta = \frac{hN}{V} . e^{\frac{\Delta G^*}{RT}} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.28)$$

Where, ΔG^* is the change of free energy of activation per mole for viscous flow, V_m is the molar volume for liquids or solutions and h, N, R and T have usual meaning. The values of change of free energy of activation (ΔG^*) can be calculated by using the Nightingle and Benck equation [50],

$$\Delta G^* = RT\ln(\frac{\eta V}{hN}) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.29)$$

And values for the corresponding thermodynamic parameters, enthalpy of activation, ΔH^* and entropy of activation ΔS^* for per mole for viscous flow of the liquids or solutions have been calculated from the relationship (1.2.28) [50]

$$\ln\frac{\eta V}{hN} = \frac{\Delta H^*}{RT} - \frac{\Delta S^*}{R} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1.2.30)$$

Assuming $\Delta H^*$and $\Delta S^*$to be almost independent in the temperature range studied, a plot of $\ln\frac{\eta V_m}{Nh}$against $\frac{1}{T}$, will give a straight line. From the slope and intercept $\Delta H^*$and ΔS^* can be determined respectively.

1.14 Viscosity Coefficients A and B Measurement

The Jones-Dole coefficient, A, reflects the effect of solute-solute interaction and B, is a measure of structural modifications induced by the solute-solvent interaction. The coefficients A and B for the electrolyte solutions can be measured by using the empirical equations of Jones-Dole [93]

$$\eta_r = 1 + A\sqrt{C} + BC \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1.2.31)$$

Where, η_r is the relative viscosity.

Relative viscosity, $\eta_r = \frac{\text{viscosity of solution, } \eta}{\text{viscosity of solvent, } \eta_0}$

The values of the coefficients *A* and *B* were obtained from the intercept and slope of the plot $\frac{\eta_r - 1}{\sqrt{C}}$ against $\sqrt{C}$ respectively.

CHAPTER II

Literature Review

2.1 Literature review

N-acetylcysteine (NAC), a sulfhydryl substance, is a derivative of amino acid L-cysteine widely used as medicine. It contains thiol and adjacent carboxylic acid group. The quantitation of thiol-disulfide oxidation-reduction potentials is a difficult task and can be achieved for limited kinds of compounds only. The formation of stable metal-thiolate complexes by NAC at electrode surfaces and the concomitant electrochemical irreversibility protect the use of standard voltammetric methods [51]. Reaction mixture analysis of thiol−disulfide equilibrium systems were done by spectroscopic methods [52]. The recently observed relationship between the basicity and oxidizability of thiolates is a remarkabletprogress in the Bio-chemistry of these compounds, providing a means to characterize the thiol-disulfide chemistry, even for compounds with more than one thiolate site [53].

Nowadays, at least 12 different biological activities have been attributed to NAC which is an acetylated amino acid with antioxidant and mucolytic characteristics. These two activities have made NAC particularly conversant in cystic fibrosis studies, where the antioxidant/reducing character of the compound is described to thrive the characteristic systemic redox imbalance state of cystic fibrosis and the mucolytic properties of the compound are shown to impede upon the congestion and inflammation correlated to this redox state. The above pharmacological versatility is undoubtedly unique, indicating that the background of its biological complexity must be sought at the sub-molecular level [54]. Mucolytic activity of NAC was used for the first time in the treatment of some respiratory diseases (e.g. chronic bronchitis) over 40 years ago [55]. Detoxifying properties of NAC were discovered in the 1970s and since then NAC was being used as an antidote in aminophen intoxication [56]. At present, it is known mainly as an antioxidant displaying direct and indirect activities [57]. Oxidative stress the imbalance between reactive oxygen species (ROS) and actions of the antioxidant network – takes part in pathogenesis of a broad spectrum of diseases including cancer, cardiovascular, arthritis, diabetes, influenza-like symptomatology as well as some lung disturbances namely pulmonary oxygen toxicity, adult respiratory distress syndrome, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis and cystic fibrosis [58].

Increasing number of publications confirm efficacy of using NAC in the above mentioned diseases[59-62].Further indications for its use include rheumatoid arthritis, plasma hyperlipoproteinaemia and adult respiratory distress syndrome[63]. NAC has also been reported to support repair processes after cytotoxic and radioactive damages in cancer therapy to remove atherosclerotic plaques [64]. Its mode of action has generally been assumed to be related to the thiol (or thiolate) site, as the key moiety of the molecule. The reported thiolate involved mechanisms are free radical scavenging [65], rupture of disulfide bonds in cross-linked mucous proteins, metal complex formation [66]. Some papers claim that NAC penetrates the cell membranes. Some others [67] deny that, on the basis of its poor (5%) bioavailability and very low alveolar concentration after oral administration [68]. The chemical properties of NAC have been characterized in terms of metal complexation constants, analytical stability in various pharmaceutical products, and protonation constants, determined by UV-pH titration and kinetic methods [69-70]. The aprotic solvent dimethylformamide (DMF), a colourless, and odorless liquid, is an organic compound with the formula $(CH_3)_2NC(O)H$, is miscible with water and the majority of organic liquids. It facilitates reactions that follow polar mechanisms such as Second order reaction [71].DMF is a good formylating agent for certain organometallic compounds. Even though formylation of some alkyllithium or Grignard reagents with DMF does not always give good yields of products due to side reactions, [72] sonication of a mixture of alkyl or aryl halide, lithium, and DMFsubstantially increases the rate of organometallic formation andyield of the formylated product [73]. Allenyl and vinyl organolithiums undergo formylation with DMF to produce good yields ofunsaturated aldehydes [74]. Alkyl halides can be easily synthesized on reaction of an alcohol with DMF and Phosgene [75]. In an analogous manner, 1-triptycyl carbinols undergo a deoxygenative rearrangement and halogenation on treatment with Thionyl Chloride–DMF [76].

In 1893, Albert Verley (8 January 1867 – 27 November 1959), a France chemist, prepared DMF by distilling a mixture of dimethylamine hydrochloride and potassium format. N-methylformamide works against a number of murine tumors *in vivo* (Sarcoma 180, M5076 ovarian sarcoma and TLX5 lymphoma) [77]. DMF is prepared by the replacement t of aminichydrogens of formamide by two methyl ($–CH_3$) groups. These results increase of electron density on the nitrogen atom [78]. A question arises how the thermodynamic properties of DMF aqueous solutions can influence a NAC’s structure when it is in this solution. Since there are a few experimental data regarding protein and amino acids in DMF aqueous solutions [79]. Water is universal solvent used in daily life and DMF is the organic solvent also extensively used in various sectors. It is obvious that NAC and DMF have some crucial properties that govern its viability and activity in biological media where water is present. As a result, its solution behavior and the related protonation state and medium-dependent physicochemical interaction and thermodynamic properties could be exciting. So investigation of interaction between NAC and water, NAC and DMF or NAC and DMF -water mixture could be quite interesting and applicable as well that has not been investigated earlier so far. To the best of our knowledge, still there is no explicit data of rheological and volumetric properties of N-Acetylcysteine in DMF and aqueous system. The purpose of this study is to evaluate the miscibility of N-Acetylcysteine in water, DMF and aqueous- DMF mixed solution systems.

2.2 Aim of the research

It is obvious that NAC has some crucial properties that govern its viability and activity in biological media. So its solution behavior and the related protonation state and medium-dependent physicochemical interaction and thermodynamic properties are the discussion point at this time. To the best of our knowledge, still there is no explicit data of rheological and volumetric properties of N-Acetylcysteine in DMF and aqueous system are available. The purpose of this study was to evaluate the miscibility of N-Acetylcysteine in water, DMF and H_2O–DMF mixed solution systems. Physico-chemical study recognized useful tool in getting sound information about the structure of various solution system. The specific aims of this study are:

i) to be aware of the probable interaction between water + N-Acetyl-L-cysteine solution, DMF + N-Acetylcysteine solution, water + DMF + N-Acetylcysteine ternary solution.

ii) to explore the role of N-Acetylcysteine in physico-chemical interactions of the systems mentioned in i).

iii) to understand the probable ion-solvent and ion-ion interactions of the investigated system.

iv) to determine the rheological properties of ternary mixture solutions (water + DMF + NAC) and the effects of binary mixture solutions (water + DMF) in various NAC concentrations will be measured by viscometry at (298.15-318.15) K.

CHAPTER III

Experimental

3.1 General

During the course of the present work a number of techniques were involved which were in general standard ones. Constant efforts for attaining the ideal conditions for the experiments were always attempted.

The thoroughly cleaned glass pieces were dried in electric oven. The smaller pieces of apparatus were dried in electric oven and stored in desiccators, while larger pieces of apparatus were used directly from the oven.

The density of pure solvents and different solutions was determined by the density and sound velocity meter (DSA-5000M). Microviscometer model (Lovis 2000 M)were used for measurement of viscosity. The capillary used for determining viscosity was cleaned thoroughly with distilled water followed by ethanol and finally with acetone and dried.

3.2 Apparatus

Viscosities of various liquids were measured using Microviscometer (Lovis 2000 M). And the densities were measured by Density and Sound Velocity Meter (DSA 5000M) Anton Paar, Austria. Electronic balance (ATX224, made in Philippine) with an accuracy of ± 0.0001g was used for weighing. The flow time of liquids were recorded by the density meter capable to read up to 0.01 seconds. The experimental temperatures were 298.15 to 323.15K at 5K intervals. Calibrated volumetric flask, pipette and burette were used for necessary volume measurement.

3.3 Preparation and Purification of Reagents

High quality analytical grade reagents were used in all the experiments and where necessary further purifications were done.

3.4 Distillation of water

First time water was distilled by water distillation apparatus. First time distilled water was further purified by a quick-fit glass made distillation apparatus. About 1.5 L water was taken in a round bottom reservoir of which the capacity was 2.0 L. Then it was distilled in presence of $KMnO_4$. Distilled water was collected at only 100°C. Other liquids of which the temperatures were below and above the mentioned boiling point were discarded. In all the experiments double distilled water was used.

3.5 Chemicals

N-acetylcysteine was collected from Sigma Aldrich, USA, High performance liquid chromatography (HPLC) grade. Dimethylformamide, $(CH_3)_2$ NC(O)H was collected from Sigma Aldrich, USA, and was 99.99% pure. All chemicals and reagents were of analytical grade and were used without further purification.

3.6 Preparation of solution

Solutions were prepared by mixing appropriate volumes of components. The volume taken by using burettes and pipettes were correct up to 0.1 cm^3. The volume of each component used as taken converted into mole fraction, special precaution was taken to prevent evaporation and introduction of moisture into the experimental samples.

3.7 Density measurement

The densities were measured by Density and Sound Velocity Meter (DSA 5000M) Anton Paar, Austria. The densities of solvents and solutions were measured separately. For this solvent and solutions were poured into the Density and Sound Velocity Meter through injection by syringe. The investigated temperatures were selected manually and the experimental data of density values were recorded automatically in the machine. Then the results were collected from the data memory. Precautions were taken in every injection and after each ejection machine was cleaned properly by ethanol, acetone on the basis of inorganic and organic solvents.

3.8 Viscosity measurement

Viscosity of water, DMF and several solutions were measured by using the Microviscometer (Lovis 2000 M).The interior of the capillary tube (set1.59) used was cleaned thoroughly with distilled water and ethanol followed by acetone, so that there was no obstruction in the capillary and the liquid could run freely without leaving any drop behind. The capillary tube was then filled with experimental solution and was inserted into the Microviscometer. The viscometer was then started. The reading at each temperature was stored from the screen of the viscometer.

Since the accurate viscosity and density of water at different temperatures are known (from literature) calibration constant A. As viscosity is measured by the following equation for different temperature,

$$\eta = A\rho t \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots (1.2.26)$$

Where, $A = \frac{\eta H_2O}{\rho H_2O \cdot tH_2O}$

Like water the flow time of different solutions were determined. Then putting the values of the calibration constant, density and time of flow of the experimental solutions, the viscosities of the solutions were determined by using the equation 1.2.26.

3.9 Apparent Molar Volume measurement:

Apparent molar volumes were determined from measured densities of solvent and solution by using the following equation 1.2.8.

$$\varphi_v = \left[\frac{1000(\rho_0 - \rho)}{C\rho_0}\right] + \frac{M_2}{\rho_0} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.8)$$

Where $\phi_v$is the apparent molar volume, *C* is the molarity, M_2 is the molecular mass of the solute (NAC), and ρ_0 and ρ are the densities of the solvent and the solution respectively. In general, ϕ_v was found to vary linearly with concentration for the systems studied. Thus, $\phi_v$data were fitted into equation1.2.14 and 1.2.19.

$$\varphi_v = \varphi_v^0 + S_v\sqrt{c} \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots \quad (1.2.13)$$

$$\varphi_v = \varphi_v^0 + S_v\sqrt{C} + b_v C \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots \quad (1.2.18)$$

Where φ_v is the apparent molar volume at infinite dilution and b_v is an experimentally determined parameter.

3.10 Determination of Thermodynamic Parameters

The values of change of free energy of activation (ΔG^*) can be calculated by using the Nightingle and Benck equation [43],

$$\Delta G^* = RT\ln\left(\frac{\eta V}{hN}\right) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.29)$$

The activation energy for viscous flow is determined from logarithmic form of Eyring equation as:

$$\ln\eta = \ln A - \frac{\epsilon_a}{RT} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.27)$$

The slope and intercept of the straight line of plot of $\ln\eta$ vs $\frac{1}{T}$ presented the values of activation energy for viscous flow and Arrhenius constant respectively.

Values of enthalpy of activation, ΔH^* and entropy of activation, ΔS^* for per mole for viscous flow of solutions have been calculated from the relationship (1.2.30)

$$\ln\frac{\eta V}{hN} = \frac{\Delta H^*}{RT} - \frac{\Delta S^*}{R} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (1.2.30)$$

Assuming ΔH^* and ΔS^* to be almost independent in the temperature range studied, a plot of $\ln\frac{\eta V_m}{Nh}$ against $\frac{1}{T}$, will give a straight line. From the slope and intercept ΔH^* and ΔS^* can be determined respectively.

CHAPTER-IV

Results and Discussion

4.1 Investigated Systems

The whole research work has been designed within six investigated systems to identify the change of interaction in various concentrations of NAC in different binary and ternary solution of DMF and water, which will provide the change of information in volumetric, viscometric and thermodynamic properties of solutions to determine the molecular interactions among NAC, DMF and water. The investigated systems are:

i) NAC–H_2O
ii) NAC–DMF
iii) NAC in [4:1] [DMF–H_2O]
iv) NAC in [3:2] [DMF–H_2O]
v) NAC in [2:3] [DMF–H_2O]
vi) NAC in [1:4] [DMF–H_2O]

4.2 Volumetric Properties

4.2.1 Density of Pure Solvent

The density at different temperatures of the pure solvents; DMF and water have been tabulated in Table 4.1 with the literature values [80, 81] for possible comparison. The larger density values of water indicate that water is denser than DMF at all investigated temperatures. From the table it is also seen that densities of the solvents decreased with the increasing temperature as expected and provide almost same results as mentioned in the cited literatures. It indicates that the solvents being used in the experiments were pure and analytical grade as declared by suppliers.

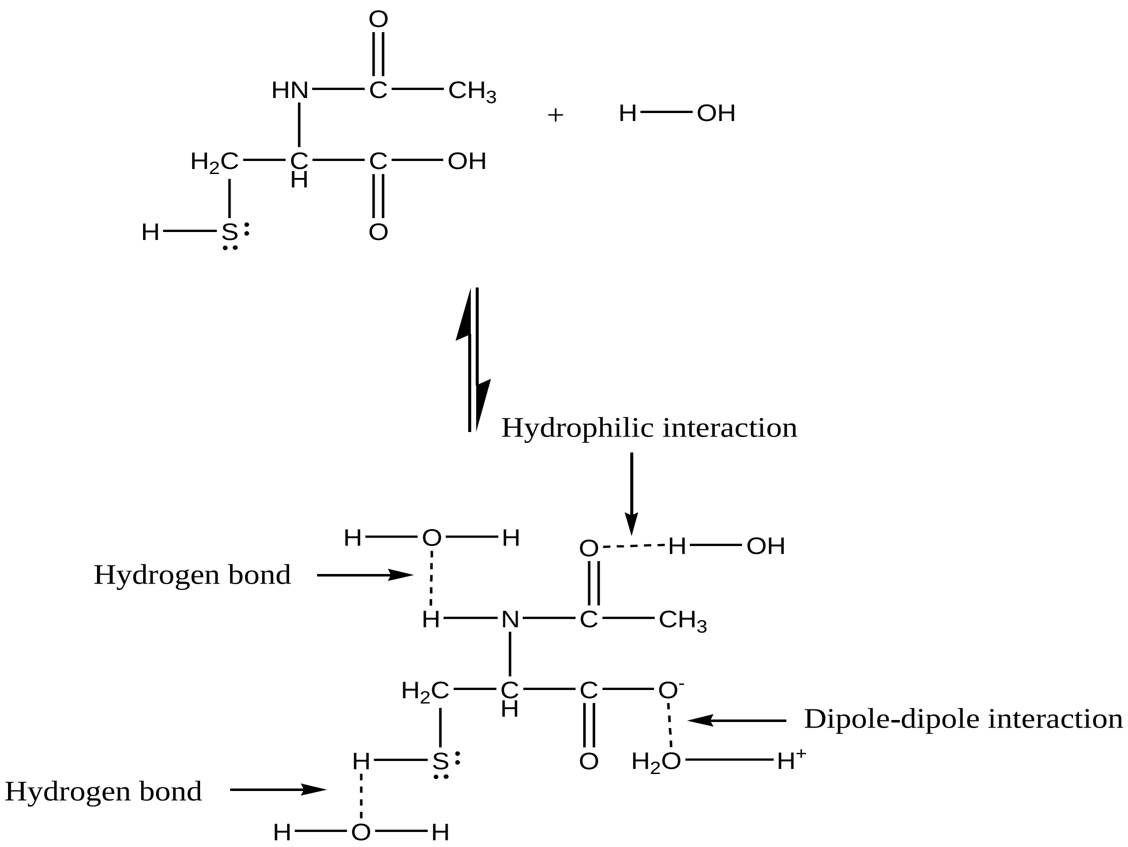
Table 4.1: Density, ρvalues of DMF and Water at 298.15 to 318.15 K at 5 K interval

Temperature (K)	Density (g/cm^3) of DMF		Density (g/cm^3) of Water	
	Literature Value	Experimental Value	Literature Value	Experimental Value
298.15	0.944061 [80]	0.945843	0.9971 [81]	0.997016
303.15	0.939376 [80]	0.941067	0.9957 [81]	0.99561
308.15	0.934402 [80]	0.936278	0.9940 [81]	0.993922
313.15	0.929860 [80]	0.931477	0.9922 [81]	0.990832
318.15	0.92502 [80]	0.92667	0.9902 [81]	0.986101

4.2.2 Density of NAC–H_2O Binary System

The density values, ρof different concentration of NAC (0.1001,0.3001,0.5006,0.7003,0.9002,1.0001) M the in water solutions have been investigated at 298.15, 303.15, 308.15, 313.15 and 318.15 K temperatures. The density values are shown in Table 4.2. The density values of (NAC–H_2O) systems at 5 investigated temperatures are higher than those of water even the values increased with increasing the amount of NAC in water. It is seen from the result that densities of aqueous NAC solution increased with increasing concentration within the investigated composition (~0.10 to ~1.00) M of NAC in water. Comparing the results in Table 4.1 with the density values of water it can be stated that density values of solution of NAC in water are higher than those of pure water. Density values of the NAC–H_2O in Table 4.2 have fitted in Figure 4.1. From the Figure 4.1 it is seen that density values of NAC in water increased linearly with the concentration of the NAC within the temperature range of 298.15 K to 318.15 K at 5 K interval. This increase in density in NAC–H_2O binary system may be due to solute-solute, solute-solvent interaction through strong hydrogen bond, dipole-dipole as well as acid-base interaction between NAC and water. Detail mechanism of dissolution of NAC in water is still unknown. It is also seen that density values of the investigated binary systems decreased with increasing temperature at a specific concentration as shown in Figure 4.2. With increasing temperature internal energy of the molecules present in the systems is increased. As we know from the first law of thermodynamics, if energy of a system is increased then work is done on the system and changed it mode of dimension blindly, *e.g.,* increase in volume, plus some heat is absorbed. In other words, heat and work are equivalent ways of changing a system's internal energy [82]. So with increasing temperature as well as the internal energy solute–solvent interaction may be weaken and the volume is increased; the resultant is the lessen of densities.Possible interactions which occurred when NAC is dissolved in aqueous solution can be described as below:

The possible interactions between NAC and Water



NAC molecules in aqueous solution behave as weak acid because of its –COOH functional group that releases proton and exhibits negative charge and producing H_3O^+ ion in solution.

$$\underset{\text{NAC}}{C_5H_9NO_3S} + H_2O \rightleftharpoons \underset{[\text{NAC}]^-}{C_5H_8NO_3S^-} + H_3O^+$$

The amide and thiol group of NAC may form H–bond as well as dipole-dipole interaction with water. The solvation system has shown above.

Table 4.2: Density values,ρof N-Acetylcysteine in water system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Density,ρ (g/cm^3)				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC–H_2O	0.1001	1.001514	1.000114	0.998434	0.995369	0.990682
	0.3001	1.010485	1.009088	1.007421	1.004399	0.999789
	0.5006	1.019448	1.018048	1.016385	1.013408	1.008878
	0.7003	1.028339	1.026936	1.025274	1.022322	1.017858
	0.9002	1.037199	1.035782	1.034105	1.031192	1.026778
	1.0001	1.041609	1.040175	1.038482	1.035566	1.031186

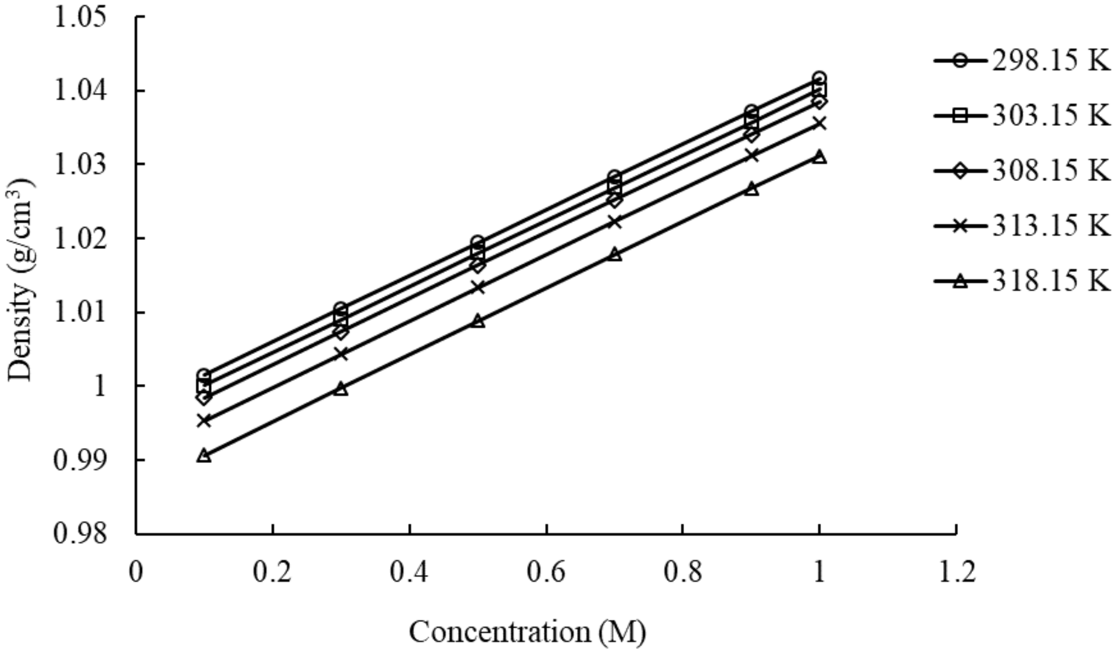


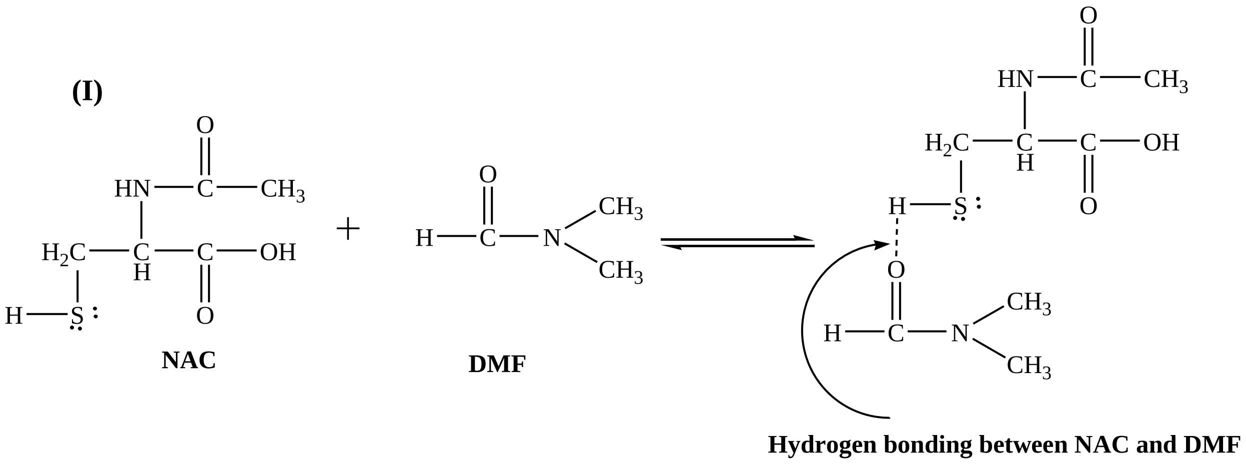
Figure 4.1: Densities, ρvs concentration (M) of N-Acetylcysteine in water system at 298.15 to 318.15 K at 5 K interval

4.2.3 Density of NAC–DMF Binary System

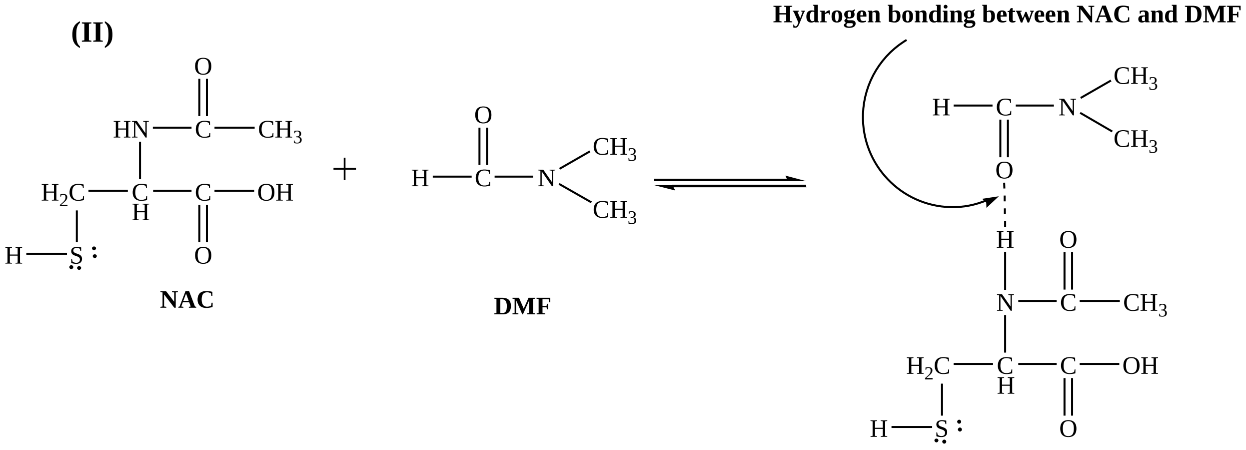
The density values, ρof different concentration of NAC (0.1001, 0.3001, 0.5004, 0.7002, 0.9002 and 1.0003) M in DMF have been investigated at 298.15, 303.15, 308.15, 313.15 and 318.15 K temperatures. The density values of NAC−DMF binary systems have been shown in Table 4.3 at different temperatures. Composition of NAC in DMF were increased from (~0.10 to ~1.00) M. From the results shown in Table 4.3and 4.1 it can be stated that density values of NAC−DMF binary solution are higher than those of the pure DMF. It is also seen that the density values of NAC solutions in DMF increased remarkably with increasing concentration at all the temperatures. The data of the Table 4.3 has been fitted in Figure 4.2. From the Figure 4.2 it is seen that density values of NAC in DMF has increased linearly with the increase in the concentration of the NAC. This increase in density of NAC−DMF binary system may be due to the solute−solvent interaction through hydrogen bond, dipole-dipole interaction between NAC and DMF. Comparing Table 4.2 and 4.3 we can see that the density values of NAC−H_2O is higher than NAC–DMFbinary. It is also seen that density values of the investigated binary systems decreased with increasing temperature at a specific concentration as shown in Figure 4.3. With increasing temperature as well as the internal energy; solute−solvent interaction may be weaken and the volume is increased; the resultant is the decrease of densities have been discussed in the earlier section 4.2.2. When NAC is dissolved in DMF following probable solvation may be occurred:

Three possible interactions between NAC and DMF

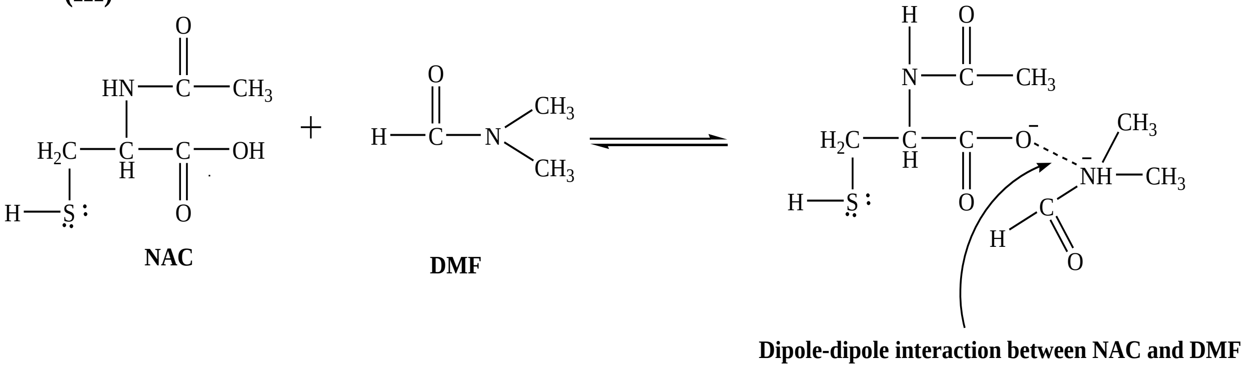
(I)



(II)



(III)



The thiol and amide groups of NAC form hydrogen bond interaction with DMF as shown in equilibrium or solvation mechanism (I) and (II), respectively. Carboxylic acid functional group of NAC molecules may release proton and the conjugate base is stabilized by $C_2H_6NC(O)H$ as shown in equilibrium or solvation mechanism (III).

Table 4.3: Density values,ρof N-Acetylcysteine in DMF system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Density, *ρ* (g/cm^3)				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC–DMF	0.1001	0.950727	0.945984	0.941229	0.936461	0.931686
	0.3001	0.960546	0.955882	0.951193	0.946497	0.941788
	0.5004	0.970423	0.965827	0.961198	0.956568	0.951938
	0.7002	0.980312	0.975785	0.971219	0.966665	0.962095
	0.9002	0.990261	0.985803	0.981295	0.976813	0.972306
	1.0003	0.995308	0.990891	0.986401	0.981938	0.977464

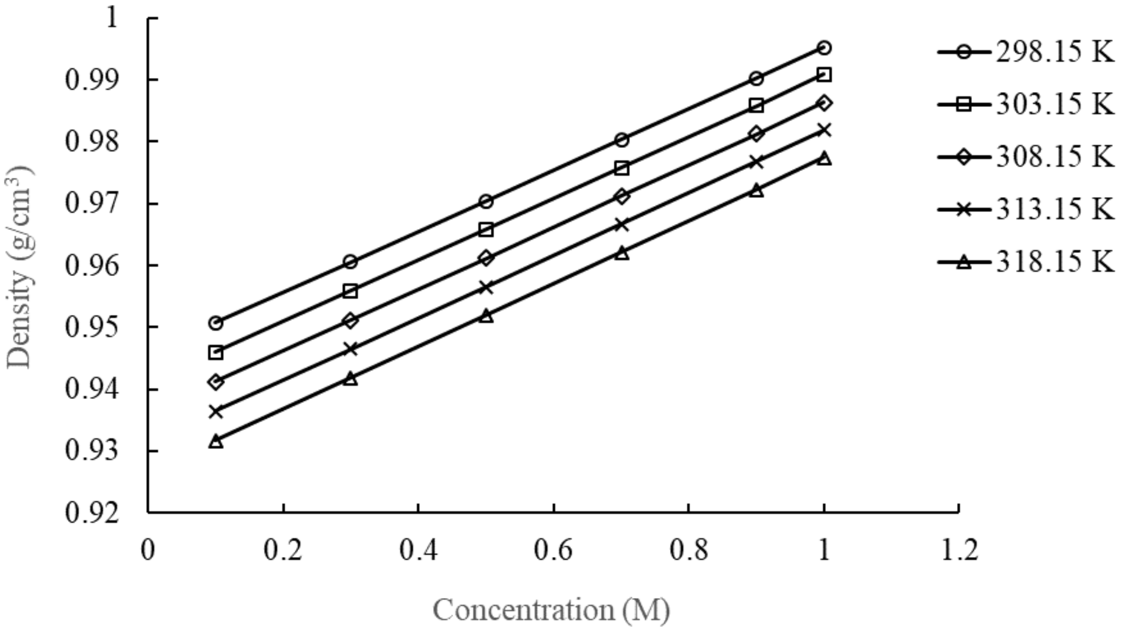


Figure 4.3: Density values, ρvs concentration (M) of N-Acetylcysteine in DMF system at 298.15 to 318.15K at 5 K interval

4.2.4 Density of DMF–H_2O Binary System

DMF–H_2O mixtures are very important systems exhibiting properties that are of great interest in physics, chemistry and biology. These include several thermodynamic and physico-chemical properties. The density values for DMF–H_2O have also been identified for further calculations as shown in the Table 4.4. With the increasing amount of DMF in the binary mixture of DMF–H_2O; the density increases. The values are larger than DMF but smaller than water.

Table 4.4: Experimental density values, ρof [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Name of the system	Experimental Value, ρ (g/cm^3)				
	298.15K	303.15K	308.15K	313.15K	318.15K
[4:1] [DMF–H_2O]	0.979115	0.974452	0.969751	0.965001	0.960215
[3:2] [DMF–H_2O]	0.994176	0.989991	0.985744	0.981438	0.977076
[2:3] [DMF–H_2O]	0.996993	0.993661	0.990235	0.986716	0.983107
[1:4] [DMF–H_2O]	0.996282	0.993998	0.991554	0.988949	0.986212

4.2.5 Density of NAC−DMF−H_2O Ternary System

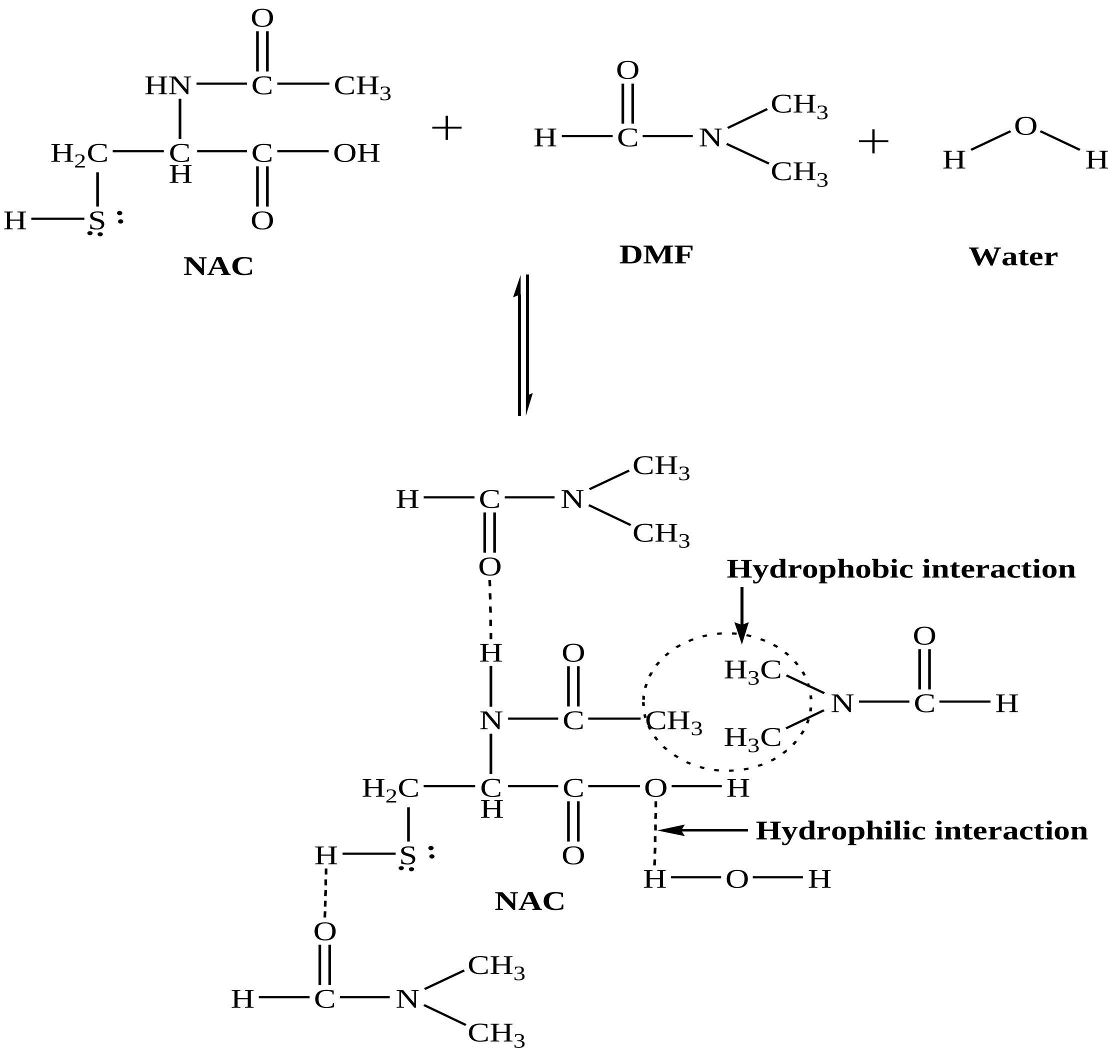
The densities, ρof the five specific concentration of NAC in [4:1], [3:2], [2:3] and [1:4] [DMF−H_2O] systems at 298.15K to 318.15 K at 5K interval has been investigated. The density values have shown in Table 4.5. The density values of NAC in [1:4] [DMF−H_2O] ternary systems are the highest than all other ternary and also than those of both NAC−H_2O and NAC−DMF binary systems. The density values increased with increasing concentration of NAC in DMF−H_2O at the entire investigated composition range, (~0.10 to ~1.00) M NAC in mixed solvents. Comparing the results in Table 4.1, 4.2, 4.3, 4.4 and 4.5 it can be stated that densities of NAC in DMF−H_2O increased remarkably with concentration at all the temperatures. The values of the Table 4.5 are fitted in Figure 4.3-4.6. From the figures it is seen that the densities of NAC in [4:1], [3:2], [2:3] and [1:4] [DMF−H_2O] systems increased linearly with the concentration of the NAC within the temperature range of 298.15 K to 318.15 K at 5 K interval. It is seen that with increasing amount of water in NAC−DMF−H_2O systems density values increased. At the same time NAC is also a polar organic solute (with –COOH, –SH, CH_3CONH–functional groups). So with increasing the ratio of water in DMF−H_2O systems amount of solvation with strong interaction took place between NAC and increased amount of water as a result densities increased. It is also seen that density values of the investigated ternary systems decreased with increasing temperature at a specific concentration as shown in Table 4.5 and Figure 4.3-4.6. It is already mentioned that with increasing temperature internal energy increased which affect or increase the vibrational, rotational and translational state of the system. As a result volume of the system increased and density values decreased.

In case of ternary systems, the highest densities observed for NAC in [1:4] [DMF−H_2O] system, probably highest dipole-dipole interactions in addition to other forces. On the other hand NAC in [4:1] [DMF−H_2O] system showed lowest interaction might be due to minimum dipole-dipole forces, comparison to other ternary systems. In ternary systems the interaction increased with the increase of the ratio of water and the order is:

NAC in [1:4] [DMF−H_2O] > NAC in [2:3] [DMF−H_2O] > NAC in [3:2] [DMF−H_2O] >NAC in [4:1] [DMF−H_2O].

Detail mechanism of dissolution or solvation of NAC in DMF−H_2O system is still unknown. Here a possible mechanism has been proposed.

The probable interactions among NAC and DMF–H_2O



Two polar solvents DMF and water present in ternary systems. In presence of NAC in polar mixtures hydrophilic and hydrophobic interaction in solvent-solvent, solvent-solute; H-bond and other forces of interaction, like van der Waal’s forces increased the interactions among the molecules and increased the density than those of the binary systems e.g., DMF–H_2O, NAC–DMF, NAC–H_2O; even the pure systems. The order density of different systems may be as follows:

NAC– H_2O> NAC in [1:4] [DMF–H_2O] > NAC in [2:3] [DMF–H_2O] > NAC in [3:2] [DMF–H_2O] >NAC in [4:1] [DMF–H_2O] > NAC–DMF

Table 4.5: Density values, ρof N-Acetylcysteine in [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Density, ρ (g/cm^3)				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC in [4:1] [DMF–H_2O]	0.10001	0.983085	0.978413	0.973708	0.968952	0.964169
	0.30021	0.991156	0.986464	0.981746	0.976964	0.972184
	0.50001	0.999427	0.994681	0.989882	0.985073	0.980303
	0.70002	1.007844	1.003068	0.998215	0.993432	0.988585
	0.90001	1.016492	1.011811	1.006978	1.002152	0.997283
	1.00001	1.020904	1.016225	1.011316	1.006577	1.001683
NAC in [3:2] [DMF–H_2O]	0.10001	0.997896	0.993692	0.989433	0.985115	0.980742
	0.30002	1.005493	1.001234	0.996957	0.992624	0.988222
	0.50012	1.013214	1.008964	1.004681	1.000356	0.995914
	0.70001	1.021169	1.016929	1.012624	1.008255	1.003832
	0.90006	1.029247	1.02501	1.02073	1.016343	1.011908
	1.00001	1.033317	1.029097	1.024772	1.020427	1.016056
NAC in [2:3] [DMF–H_2O]	0.10002	1.001171	0.997797	0.994326	0.990771	0.987132
	0.30001	1.009418	1.00596	1.002417	0.998792	0.995078
	0.50002	1.017516	1.014004	1.010355	1.006646	1.002854
	0.70002	1.025464	1.021887	1.018156	1.014445	1.010602
	0.90003	1.033388	1.029693	1.025901	1.022152	1.018301
	1.00001	1.037231	1.033522	1.029687	1.025919	1.022076
NAC in [1:4] [DMF–H_2O]	0.10001	1.000765	0.998422	0.995916	0.993258	0.990478
	0.3001	1.009627	1.007149	1.004529	1.001774	0.998915
	0.50001	1.018358	1.01578	1.01307	1.01023	1.007291
	0.70003	1.027008	1.02432	1.021518	1.018595	1.015549
	0.90004	1.035525	1.032657	1.029811	1.026802	1.023701

	1.00001	1.039655	1.036721	1.033779	1.030753	1.027638

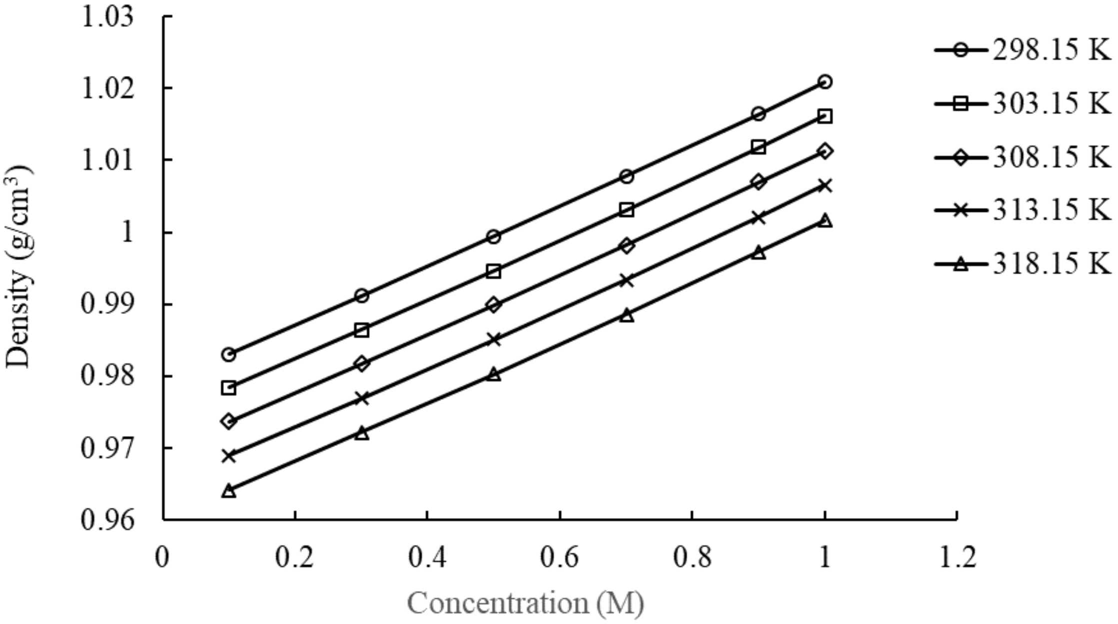


Figure 4.3: Densities, ρvs concentration (M) of N-Acetylcysteine in [4:1] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

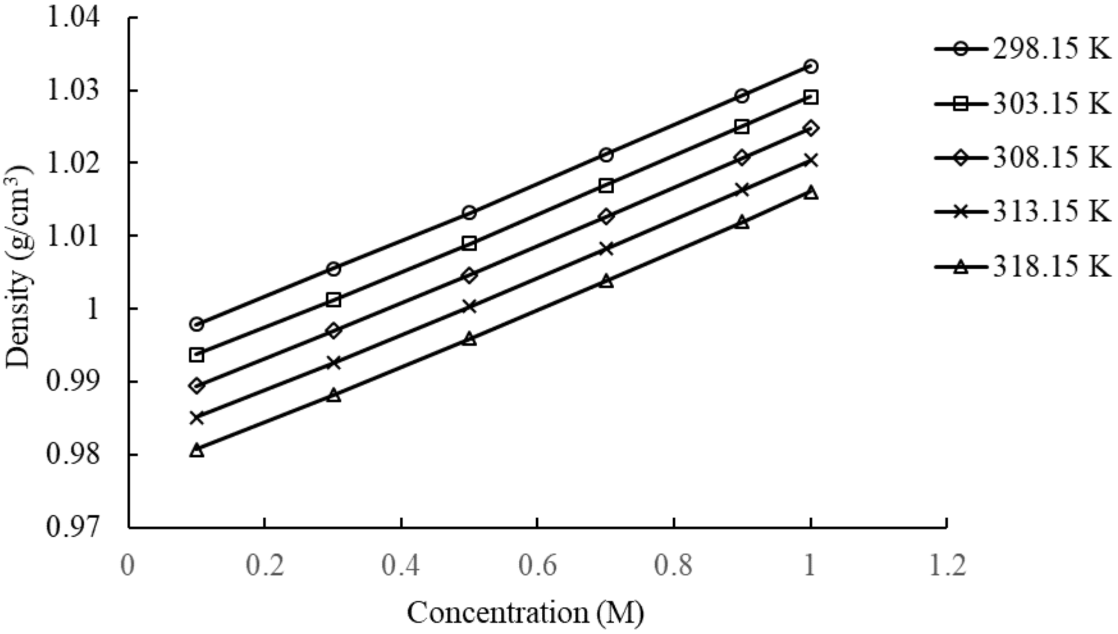


Figure 4.4: Densities, ρ vs concentration (M) of N-Acetylcysteine in [3:2] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

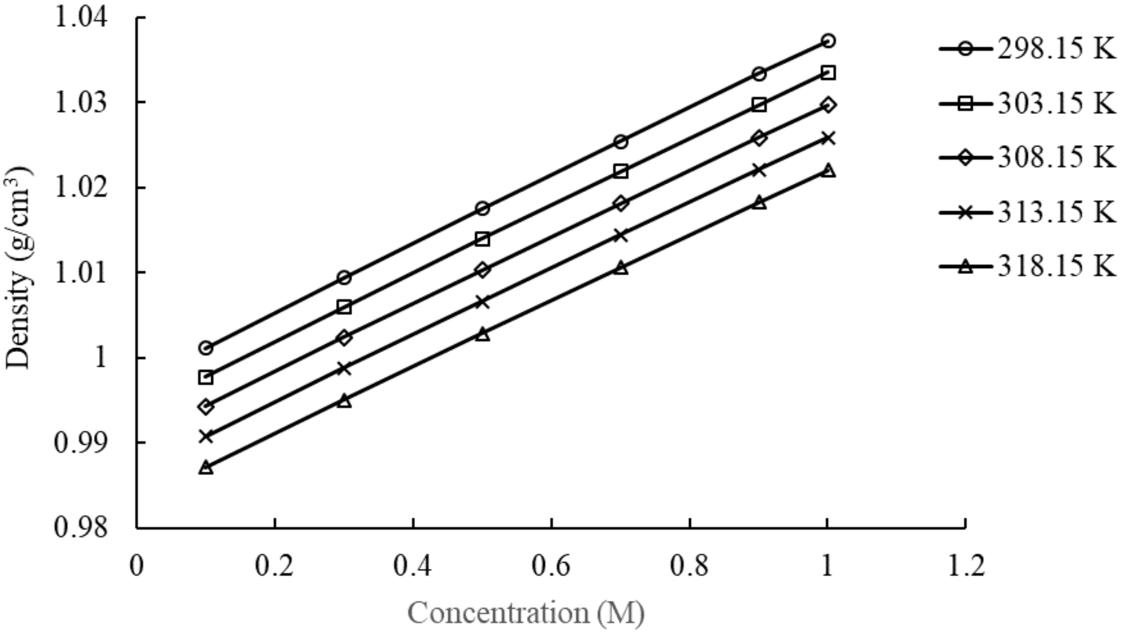


Figure 4.5: Densities, ρvs concentration (M) of N-Acetylcysteine in [2:3] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

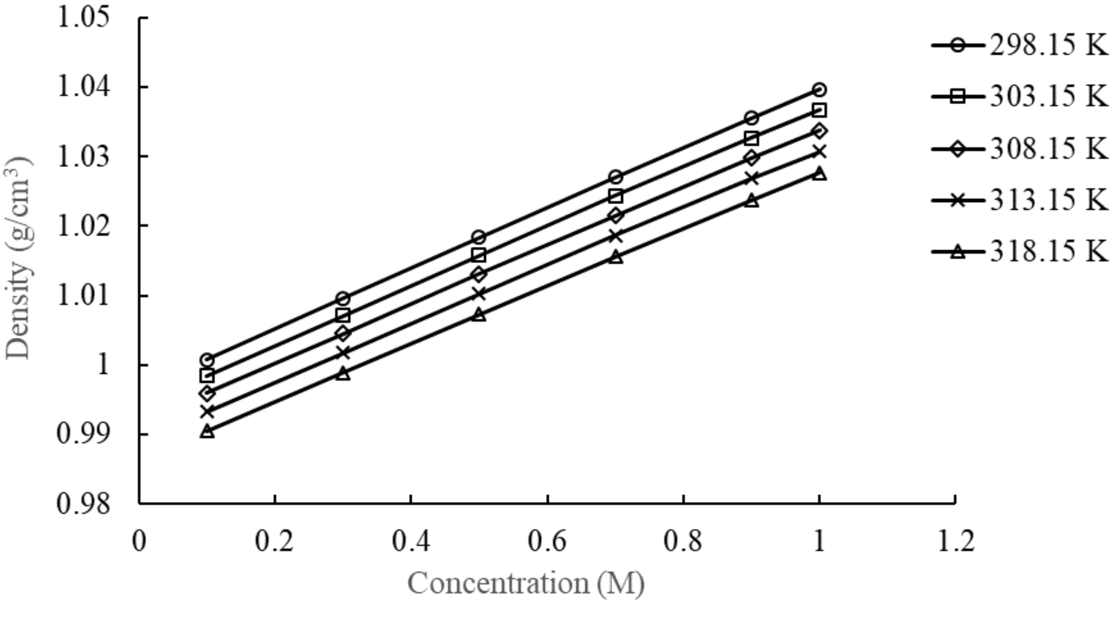


Figure 4.6: Densities, ρvsconcentration (M) of N-Acetylcysteine in [1:4] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

4.3 Apparent Molar Volume

The volumetric properties of NAC in solution can provide useful information in elucidating the interactions which occur in water, DMF as well as DMF–H_2O mixed solutions. NAC possessing both polar and non-polar groups have potential effects on the structure or molar volume of water, DMF as well as DMF–H_2O mixed solutions exhibit interactions of particular important applications. Hydrophobic interactions between the organic parts of NAC and DMF may play an important role in the stability in the mixture even when water is added to it. From a theoretical point of view, the most useful quantities are the limiting values of the apparent molar volume since these values depend only on the intrinsic size of the ion and on ion-solvent interaction. Moreover, the interactions of solutes with water may influence their accession to, and binding with, receptor sites, thus influencing their perception properties. In order to investigate the nature of the solute-solute and solute–solvent interactions of NAC in aqueous DMF solution, the apparent molar volume and apparent molar volume at infinite dilution were determined.

4.3.1 Apparent Molar Volume of NAC–H_2O Binary System

The apparent molar volume of different concentration (~0.10 to ~1.00) M of NAC in water solution has been determined at 298.15 to 318.15 K temperatures at 5K interval by using equation 1.2.8. The values of apparent molar volume of NAC–H_2O binary system has been shown in the Table 4.6. The graphical representation of the φ_v values of NAC–H_2O binary system has been shown in Figure 4.7. The apparent molar volume values vary linearly with square root of concentration of NAC solution.

It is seen that apparent molar volume is dependent upon the concentration of NAC as well as on temperature. The values have been found to be positive throughout the whole concentration range for NAC in water medium. The apparent molar volumes of NAC in water were found to be increased with the increasing concentration at all temperatures. Moreover the increase in magnitude of φ_v values with an increase in molarities of NAC suggest that the presence of ion-ion interactions [83].

The increase of apparent molar volume values of NAC with concentrations may be attributed to the increase in solvent-solvent, solute-solvent and the solute-solute interactions. In the case of solvent-solvent interaction: in H_2O–H_2O there are H-bond and dipole-dipole interaction might be present. When the concentration of NAC is increased in NAC–H_2O system it is assumed that in addition to solute-solvent interactions NAC molecules may interact through S⋯S linkage that link two molecules together, commonly termed as solute–solute interaction [84, 85]. Every S⋯S linkage is made between two molecules of NAC serves as a "staple" holding them in a more steady position.

However the φ_v values of NAC in water also increase with a rise in temperature in the system which suggests that at higher temperature significant solute-solvent interactions present in the mixtures.

Table 4.6: Apparent molar volume, $\varphi_v$of NAC in water system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Apparent molar volume, φ_v (cm^3/mol)				
		298.15K	303.15 K	308.15 K	313.1 K	318.15 K
NAC–H_2O	0.1001	118.61	118.72	118.84	118.96	119.09
	0.3001	118.67	118.80	118.94	119.08	119.24
	0.5006	118.74	118.89	119.05	119.19	119.35
	0.7003	118.82	118.99	119.15	119.32	119.51
	0.9002	118.91	119.09	119.28	119.46	119.67
	1.0001	118.96	119.16	119.36	119.56	119.78

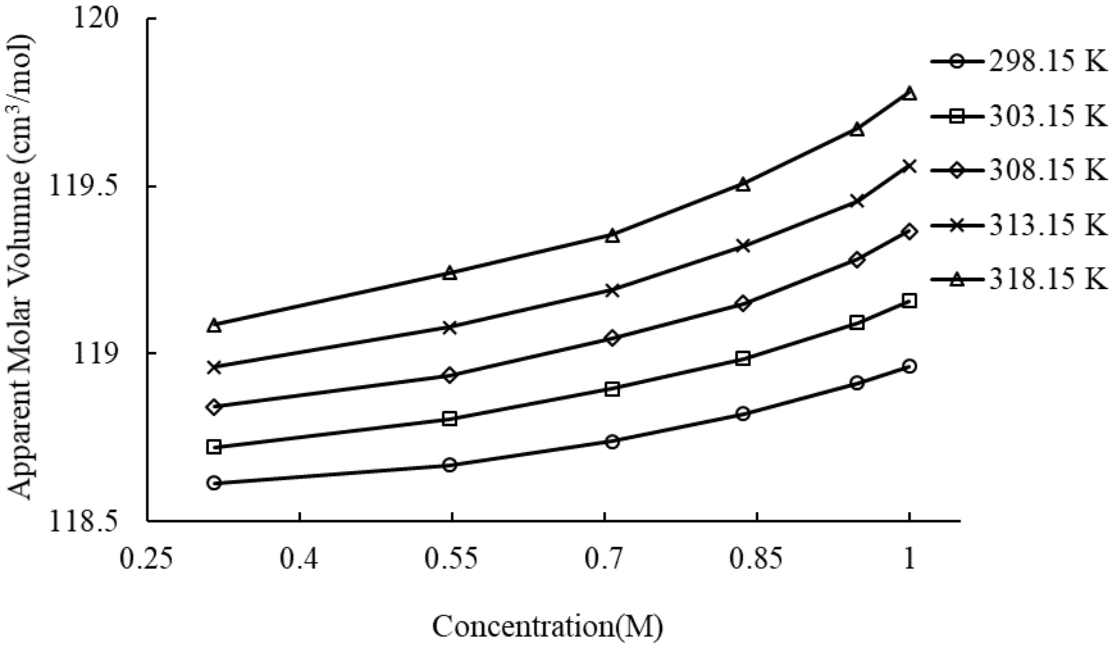


Figure 4.7: Apparent molar volume, φ_v vs concentration (M) of N-Acetylcysteine in water system at 298.15 to 318.15 K at 5 K interval

4.3.2 Apparent Molar Volume of NAC–DMF Binary System

The apparent molar volume of NAC–DMF binary system has been determined in different concentration (~0.10 to ~1.00) M of NAC from 298.15 to 318.15 K temperature at 5K interval by using equation 1.2.8. The values of apparent molar volume of NAC–DMF binary system has been shown in the Table 4.7. The graphical representation of the φ_v values of NAC–DMF binary system has been shown in Figure 4.8. The apparent molar volume decreased linearly with square root of concentration of NAC solution.

It is seen that apparent molar volume is dependent upon the concentration of NAC as well as on temperature. The values have been found to be positive throughout the whole concentration range for NAC in DMF. The apparent molar volume of NAC in DMF has been found to be decreased with the increasing concentration at all temperatures. As we know a decrease in magnitude of φ_v values with an increase in molarities of NAC suggest that the presence of ion–dipole interactions [83].

The decrease of apparent molar volume values of NAC with concentrations may be attributed to the increase in solvent-solvent and solute-solvent interactions. In the case of solvent-solvent: in DMF–DMF there are dipole-dipole and van der Waal's force of attraction might be present. It also contains hydrophobic group which interact with the hydrophobic group of NAC. As a result solute-solvent interactions increases in NAC–DMF binary system.

However the φ_v values increase with a rise in temperature in NAC–DMF system which suggests that at higher temperature significant solute-solvent interactions are present in the mixtures. It is clearly seen that, the φ_v values of NAC–DMF is the highest between binary systems at all the temperatures. The apparent molar volume, φ_v of NAC in all concentrations and temperatures in water and DMF has been found in the order of:

$$\text{NAC–DMF} > \text{NAC–}H_2O$$

Table 4.7: Apparent molar volume, $\varphi_v$of NAC in DMF system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Apparent molar volume, φ_v (cm^3/mol)				
		298.15K	303.15 K	308.15 K	313.1 K	318.15 K
NAC–DMF	0.1001	120.95	121.22	121.48	121.75	122.03
	0.3001	120.74	120.96	121.22	121.47	121.75
	0.5004	120.61	120.84	121.11	121.37	121.62
	0.7002	120.49	120.73	121.00	121.25	121.51
	0.9002	120.37	120.61	120.89	121.13	121.40
	1.0003	120.26	120.49	120.78	121.04	121.31

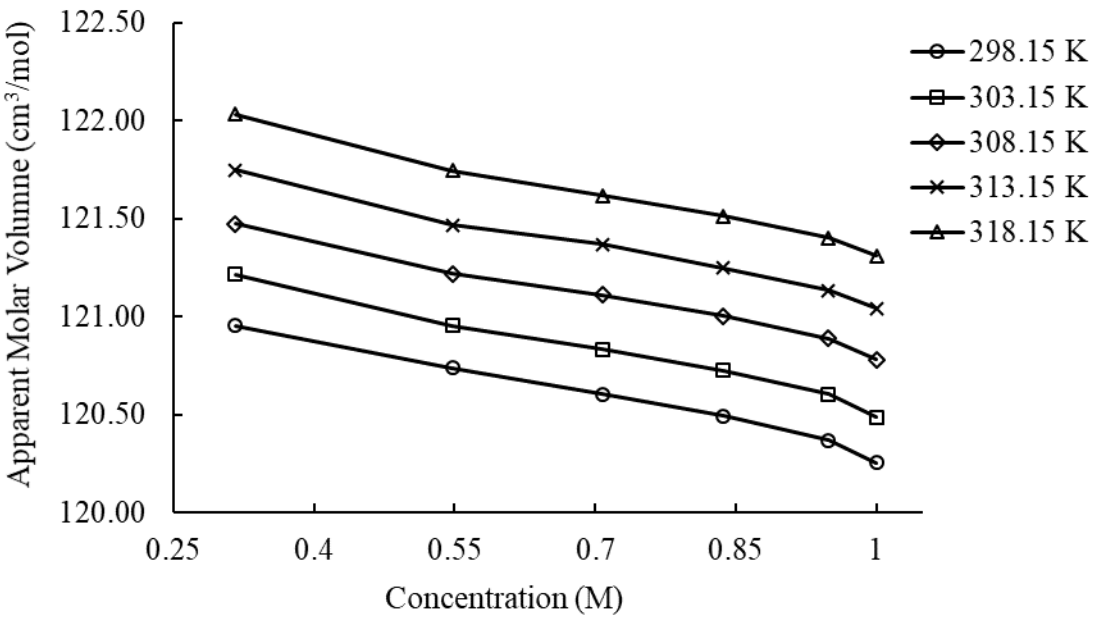


Figure 4.8: Apparent molar volume, φ_v vs concentration (M) of N-Acetylcysteine in DMF system at 298.15 to 318.15 K at 5 K interval

4.3.3 Apparent Molar Volume of NAC−DMF−H_2O Ternary System

The apparent molar volume of NAC in DMF−H_2O mixture systems have been determined at various concentration (~0.10 to ~1.00) M of NAC from 298.15 to 318.15 K temperature at 5K interval by using equation 1.2.8. The values of apparent molar volume of the ternary systems have been shown in the Table 4.8. It is seen that like binary systems, apparent molar volume is also dependent upon the concentration of NAC as well as on temperature. The values have been found to be positive throughout the whole concentration range for NAC in all ternary solution. The apparent molar volume of NAC−DMF−H_2O system has found to be decreased at [4:1] and [3:2] [DMF−H_2O] solvent systems with increasing the concentration of NAC which suggested that in addition to ion-dipole interaction, ion-ion interaction might be supplemented there but solute-solvent interaction became predominant in [4:1] and [3:2] [DMF−H_2O] solvent systems [83]. But in case of [1:4] and [2:3] [DMF−H_2O] solvent systems apparent molar volume of NAC has found to be increased which suggests that the presence of ion-ion interactions [83].

Moreover, apparent molar volumes were found to be increased with increasing temperature at any concentration of the solution and the reason has been discussed earlier for the binary systems in section 4.3.1 and 4.3.2.

The φ_v values have also found to be increased with the increase in the ratio of water in ternary systems except [1:4] [DMF–H_2O] mixture. The graphical representation of the φ_v values of ternary systems has been shown in Figure 4.9-4.12. It is seen from the Figure 4.9-4.12, the stacked line of apparent molar volumes, φ_v versus concentration of NAC in DMF–H_2O solutions; represent the trend of the contribution of each apparent molar volume over concentration. From the Figure 4.9 and 4.10 it is seen that φ_v values decrease against concentration of NAC and from Figure 4.11 and 4.12 it is seen that φ_v values increase against concentration of NAC in all cases of NAC–DMF–H_2O ternary solutions. But a remarkable increase of the φ_v properties have been seen in case of temperature.

From the above discussion about apparent molar volume reveals the following characteristics:

- Solute–solvent interaction in the NAC–DMF systems happened significantly
- Solute-solute interaction predominant in NAC–H_2O system at higher concentration of NAC
- Significant presence of solute–solute, solute–solvent interaction in the ternary systems
- H–bonding between NAC and solvents, *e.g.*, water and DMF ensued
- The apparent molar volume, φ_v are positive and large in magnitude
- φ_v increases with increasing temperature*i.e.*, temperature effect on φ_v is quite significant
- With increasing concentration of NAC, φ_v is both decreased and increased *i.e.*, concentration effect is also significant, except NAC–H_2O

Table 4.8: Apparent molar volume, $\varphi_v$of N-Acetylcysteine in [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Apparent molar volume, φ_v (cm^3/mol)				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC in [4:1] [DMF–H_2O]	0.10001	126.13	126.83	127.49	128.17	128.78
	0.30021	125.71	126.41	127.08	127.82	128.44
	0.50001	125.19	125.96	126.77	127.51	128.12
	0.70002	124.76	125.52	126.36	127.03	127.75
	0.90001	124.26	124.88	125.63	126.34	127.06
	1.00001	124.00	124.61	125.42	126.03	126.77
NAC in [3:2] [DMF–H_2O]	0.10001	126.74	127.46	128.14	128.82	129.51
	0.30002	126.21	126.99	127.64	128.29	129.00
	0.50012	125.86	126.52	127.14	127.74	128.47
	0.70001	125.36	125.97	126.60	127.25	127.90
	0.90006	124.96	125.54	126.12	126.77	127.42
	1.00001	124.78	125.34	125.96	126.56	127.13
NAC in [2:3] [DMF–H_2O]	0.10002	121.79	122.62	123.50	124.30	125.07
	0.30001	122.15	122.98	123.80	124.60	125.41
	0.50002	122.52	123.29	124.17	125.00	125.83
	0.70002	122.89	123.66	124.52	125.25	126.05
	0.90003	123.13	123.95	124.79	125.49	126.22
	1.00001	123.33	124.12	124.96	125.66	126.36
NAC in [1:4] [DMF–H_2O]	0.10001	118.81	119.68	120.60	121.45	122.22
	0.3001	119.17	120.09	120.98	121.81	122.56
	0.50001	119.49	120.35	121.19	121.98	122.73
	0.70003	119.75	120.60	121.42	122.20	122.98
	0.90004	120.04	120.97	121.72	122.49	123.24
	1.00001	120.27	121.20	122.00	122.75	123.47

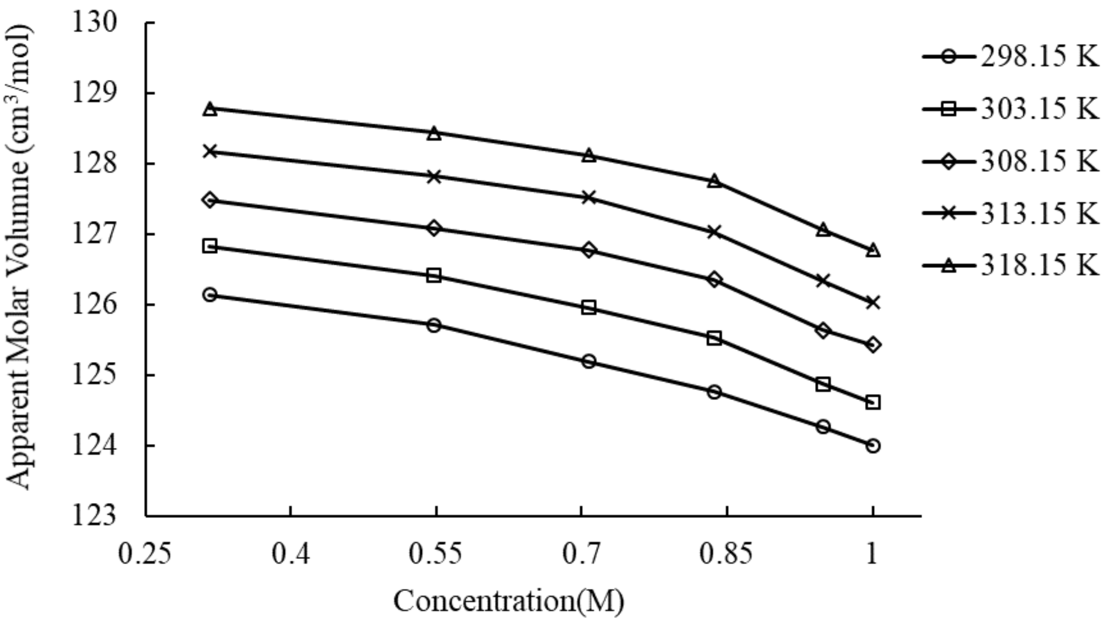


Figure 4.9: Apparent molar volume, φ_v vs concentration (M) of N-Acetylcysteine in [4:1] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

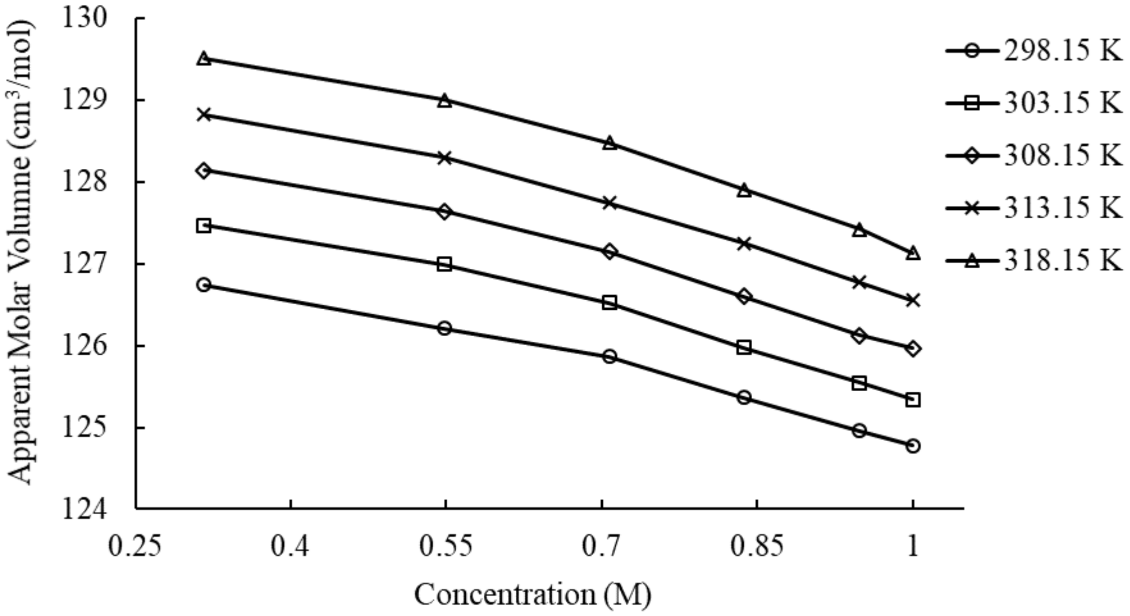


Figure 4.10: Apparent molar volume, φ_v vs concentration (M) of N-Acetylcysteine in [3:2] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

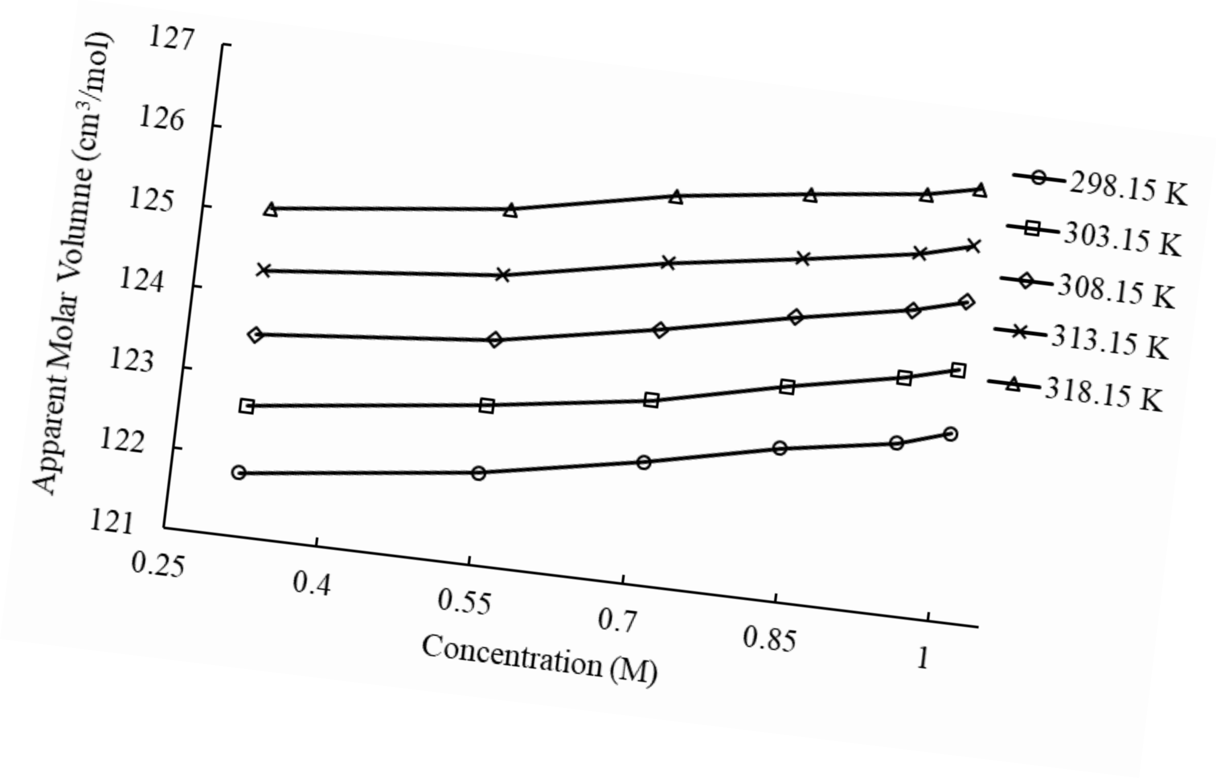


Figure 4.11: Apparent molar volume, φ_v vs concentration (M) of N-Acetylcysteine in [illegible] system at 298.15 to 318.15 K at 5 K interval

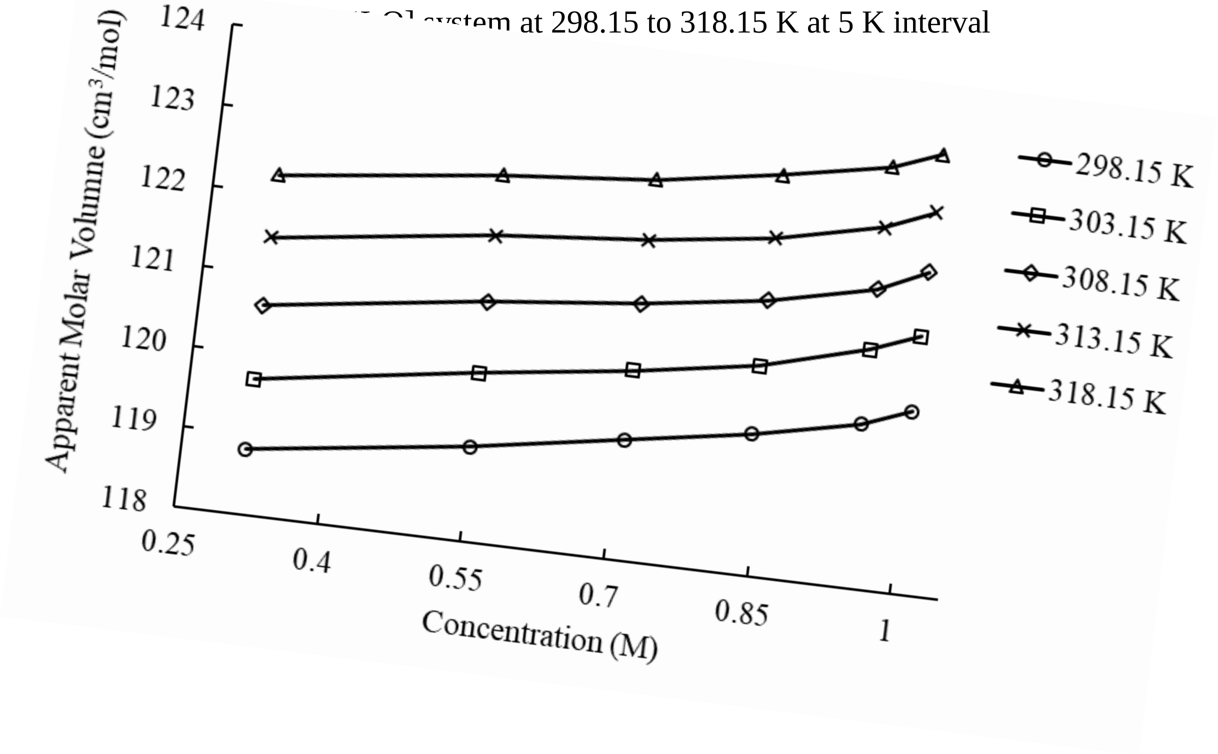


Figure 4.12: Apparent molar volume, φ_v vs concentration (M) of N-Acetylcysteine in [1:4] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

4.4 Apparent molar volume at infinite dilution

Apparent molar volume at infinite dilution, φ_v^0 varies with the molarity of NAC as represented by the following equation. The apparent molar volume at infinite dilution gives an idea about the presence of solute–solvent interactions. The S_v is the experimental slopes which give an idea about the prevailing solute–solute interactions in the mixtures. The apparent molar volumes at infinite dilution, φ_v^0 values of NAC in water, DMF and DMF–H_2O mixtures have been tabulated in Table 4.9. The results can be revealed as a function of both temperature and the structure of NAC. The φ_v^0 values of NAC reflect the true value of NAC at the specified temperatures. Apparent molar volumes at infinite dilution were computed from intercept of the plot between φ_v and $C^{1/2}$ as per following Masson equation 1.2.13.

$$\varphi_v = \varphi_v^0 + S_v\sqrt{c}$$

The apparent molar volumes, φ_v and square root of concentration, $C^{1/2}$ have been computed formerly to evaluate the value of apparent molar volume at infinite dilution which is the experimental intercept of graph between φ_v and $C^{1/2}$ and is a function of ion–solvent interactions. In case of NAC–H_2O and NAC in [1:4] and [2:3] [DMF–H_2O]solution the increase in φ_v^0values with an increase in NAC molarity represents the volume expansion [83] due to less hydrophobic interactions. In the remaining systems the decrease in the φ_v^0 values with an increase in NAC molarity represents the volume contraction [83] due to increase of hydrophobic nature of the systems. However the φ_v^0 values increase with a rise in temperature in all systems due to weaken all sorts of interactions at higher temperatures present in the mixtures.

Table 4.9: Apparent molar volume, φ_v^0 at infinite dilution of NAC in DMF, water and [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Temperature (K)	Apparent molar volume at infinite dilution, φ_v^0 (cm^3/mol)					
	NAC–H_2O	NAC–DMF	NAC in [4:1] [DMF–H_2O]	NAC in [3:2] [DMF–H_2O]	NAC in [2:3] [DMF–H_2O]	NAC in [1:4] [DMF–H_2O]
298.15	118.4138	121.2748	127.2947	127.7482	120.9882	118.0796
303.15	118.4833	121.5308	128.0655	128.6152	121.8325	118.9321
308.15	118.5553	121.7686	128.6495	129.3172	122.7065	119.9281
313.15	118.6378	122.0415	129.4082	130.0192	123.5963	120.8283
318.15	118.7195	122.3301	129.9178	130.7907	124.4329	121.6107

4.5 S_v parameter

The S_v parameter is the resultant of experimental slope of graph between φ_v and $C^{1/2}$ and is a function of ion–ion interactions. Sign of S_v gives information about the structural influence of solute on solvent system that is, whether solute acts as a structure promoting or structure breaker [86] of solvent or solvent mixture. The values of experimental slopes (S_v) have been represented in Table4.10.

The small positive values of S_v in NAC–H_2O and NAC in [1:4] and [2:3] [DMF–H_2O]solution predicts there is a strong solute-solute interaction present here whereas negative values of S_v in NAC and DMF mixtures indicate the presence of weak solute-solute interaction [87].

It is found that values of S_v are positive for NAC–H_2O, NAC in [1:4] and [2:3] [DMF–H_2O]solution and negative for NAC in DMF, NAC in[4:1] and [3:2] [DMF–H_2O] solution. It suggests that in NAC–H_2O and NAC in [1:4] and [2:3] [DMF–H_2O]solution system having more solute–solute interactions in comparison to all other systems.

Table 4.10: S_v parameter of N-Acetylcysteine in water, DMF and [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Temperature (K)	NAC–H_2O	NAC–DMF	NAC in [4:1] [DMF–H_2O]	NAC in [3:2] [DMF–H_2O]	NAC in [2:3] [DMF – H_2O]	NAC in [1:4] [DMF – H_2O]
298.15	0.5123	-0.96982	-3.14915	-2.88734	2.266843	2.077053
303.15	0.632435	-0.99931	-2.98794	-3.17886	2.208554	2.135899
308.15	0.755109	-0.94704	-2.74174	-3.28192	2.181289	1.912647
313.15	0.858769	-0.97253	-2.75112	-3.37276	2.00169	1.768366
318.15	0.992209	-0.99953	-2.54563	-3.51455	1.914371	1.7312

4.6 Viscometric Properties

Having enormous medicinal and biological applications of NAC in human body, its viscometric investigation in versatile solvent water and in common organic solvent DMF as well as in DMF–H_2O mixed solvents might be interesting. DMF–H_2O mixtures are very important systems exhibiting properties that are of great interest in physics, chemistry and biology. Due to this reason viscometric behavior of NAC in DMF, water and DMF–H_2O mixture system is also fascinating and has been discussed.

4.6.1 Viscosity of Pure Solvent

The viscosity at different temperatures of the pure solvents; DMF and water have been tabulated in Table 4.11 with the literature values [88, 81] for possible comparison. The larger viscosity values of DMF indicate that DMF is more viscous than water at all investigated temperatures. From viscosity values of DMF and water it is seen that viscosities of water are higher at all temperatures than those of DMF which correlate the density results of the solvents in Table 4.1. From the table it is also seen that viscosities of the solvents decreased with the increasing temperature as expected and provide almost similar results as mentioned in the cited literatures. It indicates that the solvents being used in the experiments were pure and analytical grade as declared by suppliers.

Table 4.11: Viscosity, ηvalues of DMF and Water at 298.15 to 318.15 K at 5 K interval

Temperature (K)	Viscosity (mPa.s) of DMF		Viscosity (mPa.s) of Water	
	Literature Value	Experimental Value	Literature Value	Experimental Value
298.15	0.790 [88]	0.877	0.8926 [96] [81]	0.859
303.15	0.750 [88]	0.824	0.8007 [96] [81]	0.775
308.15	0.710 [88]	0.773	0.7234 [96] [81]	0.701
313.15	0.681 [88]	0.726	0.6579 [96] [81]	0.639
318.15	0.642 [88]	0.686	0.6017 [96] [81]	0.587

4.6.2 Viscosity of DMF–H_2O Binary System

The viscosities of DMF–H_2O binary mixture has been shown here in Table 4.12. The values increase with the amount of DMF increases in [DMF–H_2O] except [4:1] mixture. It shows maximum value for [3:2] [DMF–H_2O] mixture solution in lower temperature (298.15K, 303.15K and 308.15K).

Table 4.12: Experimental viscosity values, ηof [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Name of the system	Experimental Value, η (mPa.s)				
	298.15K	303.15K	308.15K	313.15K	318.15K
[4:1] [DMF–H_2O]	1.946	1.716	1.525	1.343	1.121
[3:2] [DMF–H_2O]	2.546	2.184	1.882	1.606	1.414
[2:3] [DMF–H_2O]	1.959	1.701	1.491	1.318	1.172
[1:4] [DMF–H_2O]	1.321	1.167	1.038	0.931	0.839

4.6.3 Viscosity of NAC–H_2O and NAC–DMF Binary Systems

The viscosities, η of binary system NAC–H_2O and NAC–DMF have been studied at 298.15, 303.15, 308.15, 313.15, and 318.15 K temperature over a concentration range of (~0.10 to ~1.00) M of NAC. The experimented results are tabulated in Table 4.13. The viscosity values in NAC–$H_2O$and NAC–DMF systems increased with the increase of concentration as expected and the graphical presentation has been shown here in Figure 4.13 and 4.14. The values of the binary systems are also greater than the values of the pure solvents which have been shown in Table 4.11. The increase of η values of NAC with concentration can be attributed to the increase in both solute–solvent, solvent–solvent and solute–solute interactions in solution. The wide range of dissolution of NAC in water and DMF might have intriguing aspects which may be the consequence of the great ability of both water and DMF to make dipole-dipole, ion-dipole and hydrogen bonds with NAC. It is also seen that the viscosity of NAC–DMF systems are higher at all temperatures and at all concentrations of NAC than those of NAC–H_2O systems except 298.15 K temperature. This is may be due the presence of hydrophobic nature in NAC and DMF in addition to the above mentioned interactions. At the same time it is seen that the viscosity values decrease considerably with the rise in temperature at a constant molarity. In both cases with the increase of temperature in binary systems the internal energy of the system increased and as because of this the solute-solute or solute-solvent interaction may be depleted. The graphical presentation of the fact has been viewed in Figure4.13 and 4.14.

So in the measurement of viscous property in binary systems both NAC–H_2O and NAC–DMF systems show the same character but in different amount and the order of the viscosity maxima is as follows:

NAC–DMF > NAC–H_2O

Table 4.13: Viscosities, η of N-Acetylcysteine in water and DMF system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Viscosity, η (mPa.s)				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC– H_2O	0.1001	0.895	0.803	0.726	0.661	0.605
	0.3001	0.969	0.869	0.784	0.712	0.649
	0.5006	1.051	0.936	0.842	0.765	0.697
	0.7003	1.141	1.016	0.909	0.821	0.746
	0.9002	1.257	1.116	1.001	0.903	0.816
	1.0001	1.326	1.177	1.051	0.946	0.855
NAC–DMF	0.1001	0.891	0.836	0.795	0.755	0.718
	0.3001	1.102	1.042	0.986	0.925	0.87
	0.5004	1.299	1.215	1.133	1.062	0.997
	0.7002	1.531	1.436	1.331	1.248	1.166

	0.9002	1.725	1.605	1.487	1.386	1.298
	1.001	1.892	1.747	1.626	1.515	1.421

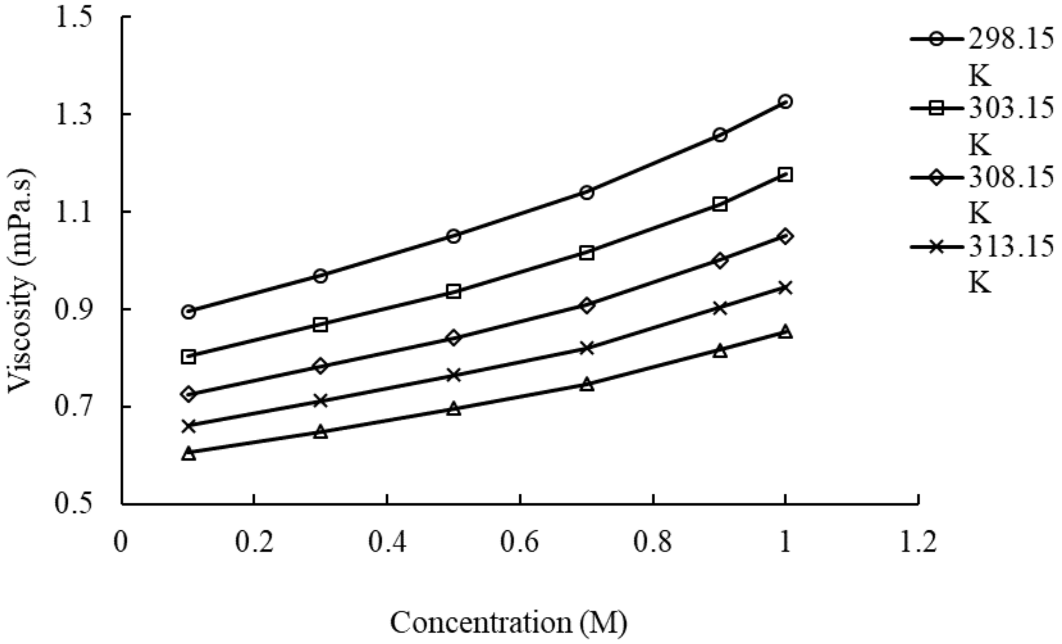


Figure 4.13: Viscosities, ηvs concentration (M) of N-Acetylcysteine in water system at 298.15 to 318.15 K at 5 K interval

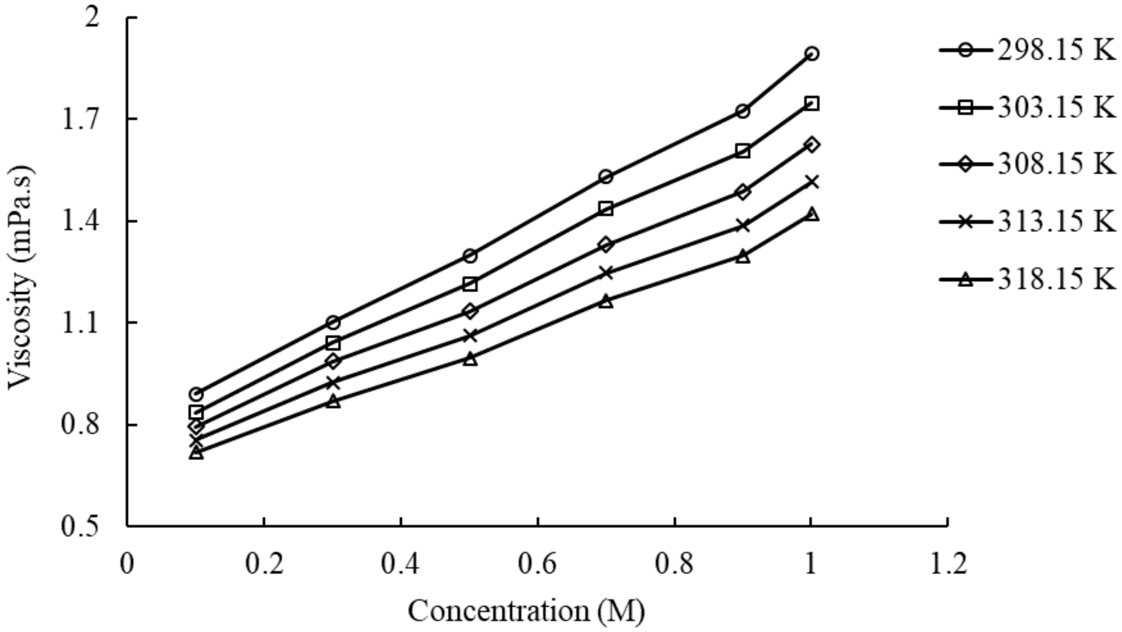


Figure 4.14: Viscosities, η vs concentration (M) of N-Acetylcysteine in DMF system at 298.15 to 318.15 K at 5 K interval

4.6.4 Viscosity of NAC–DMF–H_2O Ternary Systems

The viscosities, η of NAC in [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems have been described at 298.15, 303.15, 308.15, 313.15, and 318.15 K temperature over a concentration range of (~0.10 to ~1.00) M. The values of the viscosity of ternary systems have been tabulated in Table4.14. The results are also presented graphically in Figure 4.15, 4.16, 4.17 and 4.18. From the table we can see that the viscosity values are positive in all ternary systems and are greater than (NAC–DMF and NAC–H_2O) binary systems as shown in Table 4.13 and even those of the solvents (Table 4.11). So there may be much more solute-solute or solute-solvent interactions in the ternary systems than the others. Viscosity values increased significantly with the increase in concentration of NAC. At the same time it is seen that the viscosity values decreased considerably with temperature at a constant molarity as expected. The reason is been discussed earlier in the section 4.7.3. The reason of more interactions in ternary systems may be due to the fact that DMF, water and DMF–H_2O systems can be stabilized by hydrogen-bonded structure. Also each DMF consists of two methyl group which provide hydrophobic interaction with NAC. Thus the solubility of ternary solution is therefore become facile or make available more of the interactions and offer more organized structures. At the same time the polar groups of NAC get easily mixed with the polar solvent H_2O. It dissolves in water in any amount. On the other hand NAC contains two polar groups; –COOH and CONH–. It also contains almost nonpolar –SH group. Using this NAC make strong interactions in NAC–H_2O or NAC–DMF binary and NAC–DMF–H_2O ternary systems. In case of ternary, binary and solvent systems the viscosity maxima follow the order:

NAC in [3:2] [DMF–H_2O] > NAC in [4:1] [DMF–H_2O] > NAC in [2:3] [DMF–H_2O] > NAC in [1:4] [DMF–H_2O] > NAC–DMF > NAC–H_2O

Table 4.14: Viscosities, $\eta$of NAC in [3:2], [4:1], [2:3] and [1:4] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Viscosity, η (mPa.s)				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC in [4:1] [DMF–H_2O]	0.10001	2.321	2.053	1.811	1.607	1.439
	0.30021	2.438	2.161	1.903	1.699	1.528
	0.50001	2.721	2.386	2.109	1.878	1.681
	0.70002	3.071	2.688	2.368	2.101	1.872
	0.90001	3.342	2.991	2.612	2.296	2.031
	1.0001	3.581	3.225	2.848	2.451	2.213
NAC in [3:2] [DMF–H_2O]	0.10001	2.497	2.171	1.891	1.656	1.461
	0.30002	2.839	2.459	2.131	1.862	1.645
	0.50012	3.103	2.642	2.277	1.985	1.715
	0.70001	3.378	2.949	2.541	2.219	1.952
	0.90006	3.521	3.146	2.711	2.348	2.048
	1.00001	3.625	3.254	2.856	2.456	2.123
NAC in [2:3] [DMF–H_2O]	0.10002	1.986	1.726	1.514	1.335	1.191
	0.30001	2.145	1.862	1.625	1.426	1.262
	0.50002	2.304	1.998	1.741	1.528	1.348
	0.70002	2.471	2.135	1.857	1.631	1.443
	0.90003	2.818	2.414	2.078	1.806	1.584
	1.00001	3.052	2.654	2.312	1.985	1.757
NAC in [1:4] [DMF–H_2O]	0.10001	1.388	1.231	1.093	0.977	0.88
	0.30001	1.482	1.305	1.157	1.035	0.932
	0.50001	1.586	1.391	1.233	1.101	0.988
	0.70003	1.727	1.512	1.335	1.191	1.066
	0.90004	1.864	1.632	1.452	1.295	1.156
	1.00001	1.985	1.765	1.552	1.403	1.263

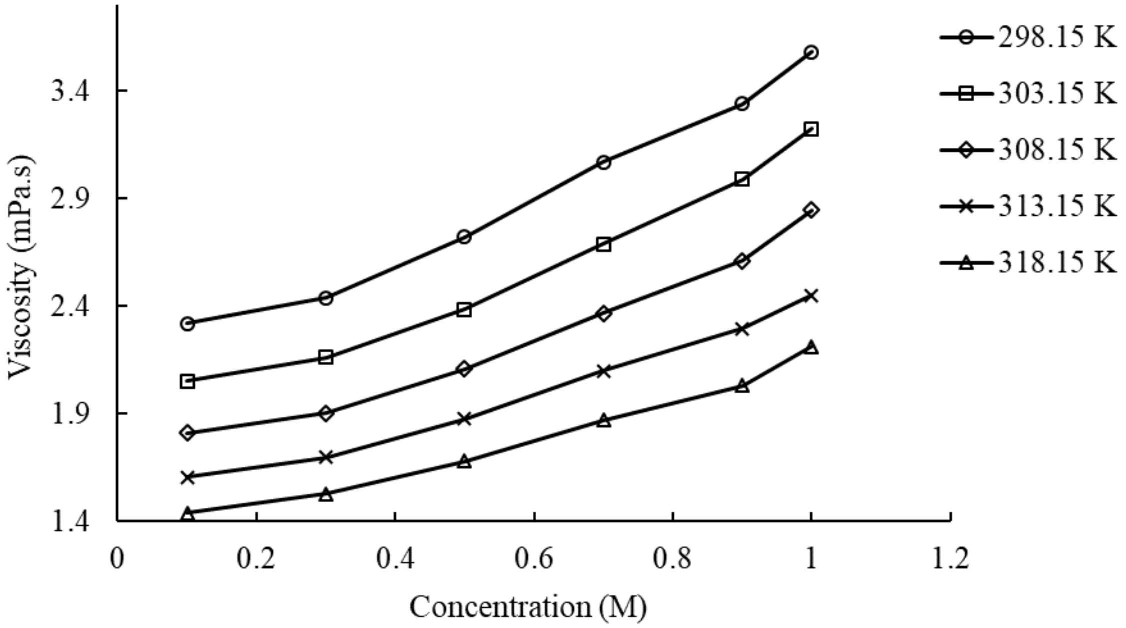


Figure 4.15: Viscosities, η vs concentration (M) of N-Acetylcysteine in [4:1] DMF–H_2O system at 298.15 to 318.15 K at 5 K interval

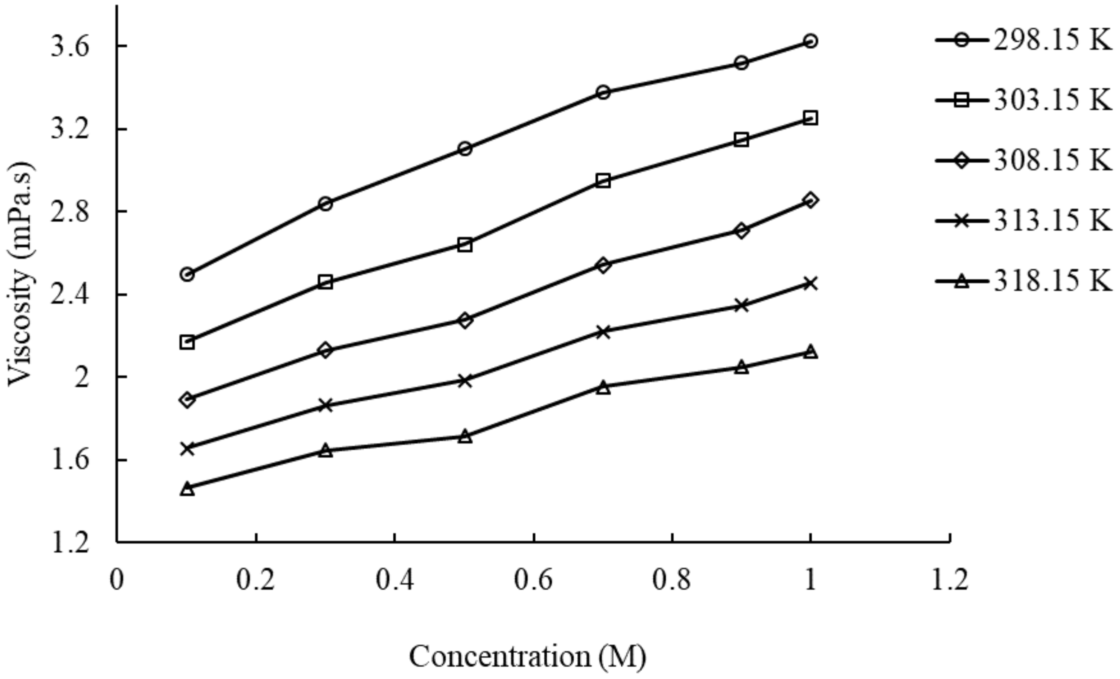


Figure 4.16: Viscosities, η vs concentration (M) of N-Acetylcysteine in [3:2] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

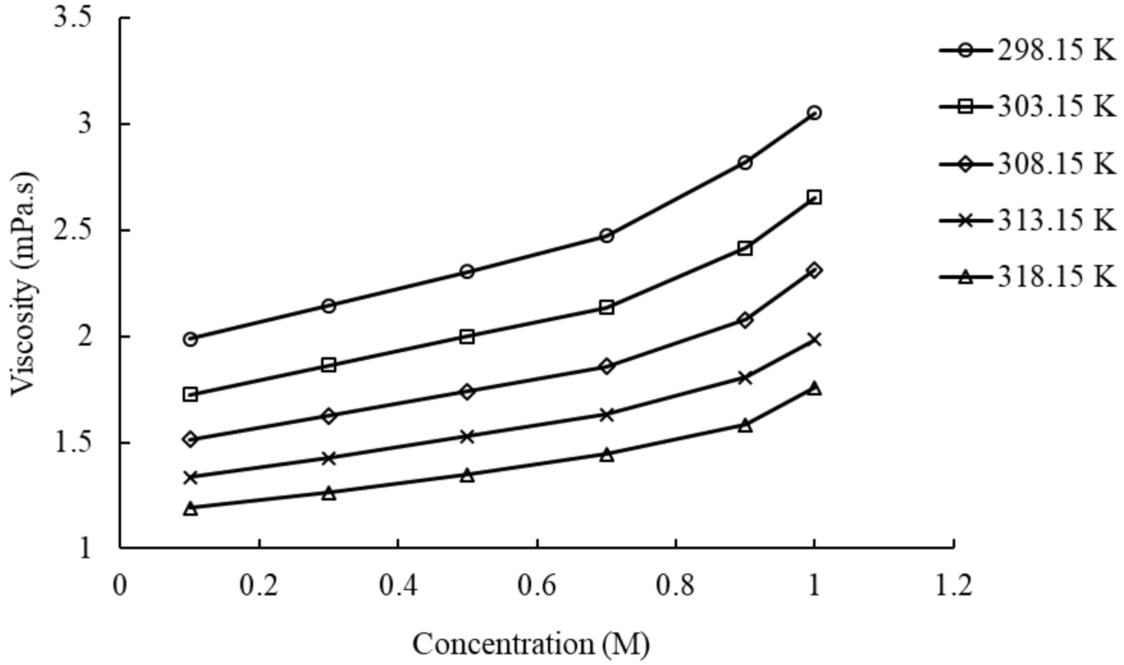


Figure 4.17: Viscosities, η vs concentration (M) of N-Acetylcysteine in [2:3] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

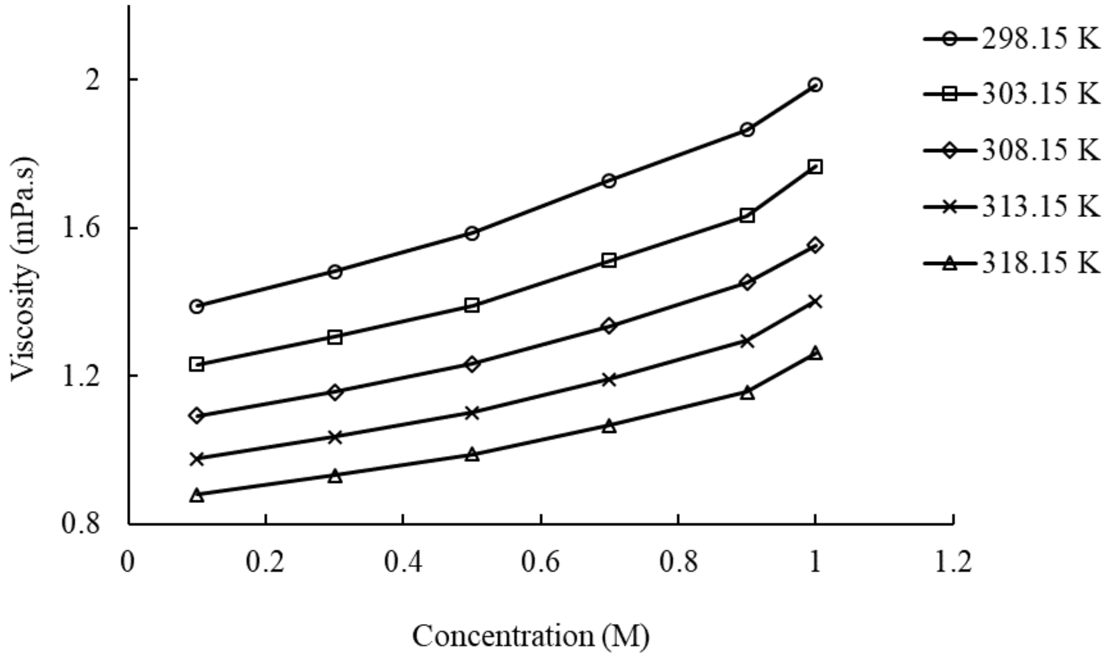


Figure 4.18: Viscosities, η vs concentration (M) of N-Acetylcysteine in [1:4] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

4.7 Jones-Dole co-efficient

The Jones-Dole co-efficient, A, reflects the effect of solute-solute interaction and B, is a measure of structural modifications induced by the solute-solvent interaction. The viscosity co-efficient A and B were obtained from the intercept and slope of the plots $(\eta_{rel} -1)/C^{1/2}$ against $C^{1/2}$. The values of A and B are listed in Table 4.15-4.17 shows that the values of A co-efficient are negative whereas those of B co-efficient are positive [89]. Values of A co-efficient are negative for all systems at all the investigated temperatures except [4:1] [DMF–H_2O] solution. These results indicate the presence of weak solute-solute interactions. The positive values of B co-efficient point out the existence of strong ion-solvent interaction in the investigated systems at the all specific temperatures. The values of B co-efficient for all solutions are lower at higher temperature that proves the decrease of ion-solvent interaction at higher temperature.

Table 4.15: Jones-Dole co-efficient for NAC–H_2O and NAC–DMF

Temperature (K)	NAC–H_2O		NAC–DMF	
	A co-efficient	B co-efficient	A co-efficient	B co-efficient
298.15	-0.07795	0.59074	-0.42112	1.559034
303.15	-0.08881	0.577431	-0.39733	1.512472
308.15	-0.08177	0.552774	-0.32593	1.410599
313.15	-0.07732	0.531553	-0.27798	1.343215
318.15	-0.08245	0.514216	-0.25068	1.292028

Table 4.16: Jones-Dole co-efficient for NAC in [4:1] and [3:2] [DMF–H_2O]

Temperature (K)	NAC in [4:1] [DMF–H_2O]		NAC in [3:2] [DMF–H_2O]	
	A co-efficient	B co-efficient	A co-efficient	B co-efficient
298.15	0.3687	0.392299	-0.2178	0.684821
303.15	0.361108	0.41761	-0.21443	0.726965
308.15	0.334175	0.42728	-0.18401	0.701895
313.15	0.405417	0.305233	-0.07639	0.609186
318.15	0.715549	0.138491	-0.05579	0.566473

Table 4.17: Jones-Dole co-efficient for NAC in [2:3] and [1:4] [DMF–H_2O]

Temperature (K)	NAC in [2:3] [DMF–H_2O]		NAC in [1:4] [DMF–H_2O]	
	A co-efficient	B co-efficient	A co-efficient	B co-efficient
298.15	-0.21047	0.702706	-0.02507	0.486672
303.15	-0.20225	0.685586	-0.01655	0.469589
308.15	-0.19337	0.658599	-0.01955	0.463059
313.15	-0.18488	0.620958	-0.03773	0.481497
318.15	-0.17211	0.592803	-0.0361	0.470923

4.8 Thermodynamic Properties

The change in viscosity of NAC in different solvents can make a significant contribution to thermodynamic properties of the solution, such as enthalpy, entropy, and other properties in solution. So in this section different thermodynamic parameters such as, change of free energy, ΔG*, change of enthalpy, ΔH*, change of entropy, ΔS* for viscous flow for NAC in different solvent systems have been discussed.

NAC–DMF, NAC–H_2O and NAC–DMF–H_2O are considered to be very important systems exhibiting properties that are of great interest in many biological and medicinal applications. These include several thermodynamic properties such as, free energy, entropy, enthalpy, etc. Thermodynamic properties, change of free energy, ΔG*, change of enthalpy, ΔH*, change of entropy, ΔS* for viscous flow have been calculated from viscometric data via Eyring equation. Gibbs free energy is a thermodynamic function and the energy of the system which is ready to work. The Gibbs free energy is used when considering processes that occur under constant pressure and temperature conditions. For a process that occurs at constant temperature and pressure, spontaneity can be determined using the change in Gibbs free energy, which is given by the sign, ΔG; depends on the changes in enthalpy (ΔH) and entropy (ΔS), as well as on the absolute temperature (T).

In cases where ΔG [90] is:

- Negative, the process is spontaneous and may proceed in the forward direction as written.
- Positive, the process is non-spontaneous as written, but it may be proceed spontaneously in the reverse direction.
- Zero, the process is at equilibrium, with no net change taking place over time.

The ΔG*, values are positive for all the studied systems NAC–DMF, NAC–H_2O and NAC–DMF–H_2O indicate that studied systems are non-spontaneous for the flow process as shown in Table 4.18 and 4.19 and it is spontaneous in the reverse direction. The positive free energy change, ΔG* for viscous flow may be interpreted by Furth model [91] which states that kinetic species involved in forming holes in the investigated solution systems may be stated by the work is required in forming the holes against surface tension of the solution. Positive ΔG* values also explain the interstitial incorporation, solute–solvent interaction that render the binary and ternary systems are more structured.

Enthalpy is the thermodynamic quantity equivalent to the total heat content of a system. It is defined as the sum of internal energy of a system and the product of the pressure and volume of the system or pressure-volume work. Internal energy is the sum of translational energy, rotational energy, vibrational energy and the kinetic energy of a matter. The change in enthalpy is the sum of the change in the internal energy and the work done. Entropy is a measure of disorder or randomness of a system. In other words, it's a measurement of the degree of randomness of energy in a system. An ordered system has low entropy. A disordered system has high entropy.

The set of rules can be used to determine four distinct cases by examining the signs of the ΔS and ΔH [90].

- When $\Delta S > 0$ and $\Delta H < 0$, the process is always spontaneous as written.
- When $\Delta S < 0$ and $\Delta H > 0$, the process is never spontaneous, but the reverse process is always spontaneous.
- When $\Delta S > 0$ and $\Delta H > 0$, the process will be spontaneous at high temperatures and non-spontaneous at low temperatures.
- When $\Delta S < 0$ and $\Delta H < 0$, the process will be spontaneous at low temperatures and non-spontaneous at high temperatures.
- For the latter two cases, the temperature at which the spontaneity changes will be determined by the relative magnitudes of ΔS and ΔH.

The change enthalpy, ΔH* values are positive for all the studied system as shown in Table 4.20-4.21. The positive ΔH values indicate that work has to be done for all the investigated systems. That is, the viscous flow is not thermodynamically favored for the systems studied. The change of entropy, ΔS* of the investigated systems are shown in same Table 4.20-4.21. The ΔS* values are positive for all the systems studied except NAC–DMF system. This means that except NAC–DMF system other binary and ternary systems are random than those of the pure one. Here one point may be remarked that as

ΔS > 0 and ΔH > 0, so the processes (except NAC–DMF systems) will be spontaneous at high temperatures and non-spontaneous at low temperatures. In case of my studied temperatures these systems were found to be non-spontaneous. The negative entropy of NAC–DMF mixtures arises due to the interplay between the relative strengths of the DMF–DMF, DMF–H_2O, H_2O–H_2O and hydrogen bonds. Thiol group of NAC molecule undergoes dipole-dipole interaction with DMF. The oxygen of carbonyl group pulls the electron towards itself and hold negative charge. Lone pair electrons of nitrogen atom fill up the electron deficiency of carbonyl carbon. The structure established H-bond with water.

Table 4.18: Free energy, ΔG* of N-Acetylcysteine in water and DMF system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Free energy, ΔG* KJ/mol				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC–H_2O	0.1001	14.6392	14.6149	14.6020	14.6029	14.6145
	0.3001	14.8361	14.8140	14.7989	14.7964	14.8002
	0.5006	15.0375	15.0012	14.9818	14.9833	14.9890
	0.7003	15.2412	15.2079	15.1779	15.1672	15.1687
	0.9002	15.4812	15.4445	15.4249	15.4151	15.4059
	1.0001	15.6136	15.5786	15.5498	15.5362	15.5294
NAC–DMF	0.1001	14.7587	14.8584	14.9877	15.1099	15.2319
	0.3001	15.2856	15.4136	15.5393	15.6386	15.7398
	0.5004	15.6932	15.8007	15.8954	15.9982	16.1002
	0.7002	16.1006	16.2219	16.3080	16.4183	16.5144
	0.9002	16.3963	16.5023	16.5919	16.6914	16.7981
	1.001	16.6254	16.7160	16.8209	16.9231	17.0376

Table 4.19: Free energy, ΔG*of NAC in [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc. (mol/L)	Free energy, ΔG* KJ/mol				
		298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
NAC in [4:1] [DMF–H_2O]	0.10001	17.0013	16.9808	16.9439	16.9158	16.9064
	0.30021	17.1233	17.1100	17.0708	17.0607	17.0652
	0.50001	17.3955	17.3596	17.3341	17.3215	17.3176
	0.70002	17.6954	17.6600	17.6309	17.6136	17.6022
	0.90001	17.9051	17.9292	17.8822	17.8447	17.8179
	1.0001	18.0763	18.1191	18.1038	18.0148	18.0449
NAC in [3:2] [DMF–H_2O]	0.10001	17.1825	17.1216	17.0546	16.9940	16.9466
	0.30002	17.5007	17.4356	17.3607	17.2992	17.2603
	0.50012	17.7211	17.6165	17.5305	17.4658	17.3706
	0.70001	17.9316	17.8936	17.8115	17.7559	17.7129
	0.90006	18.0344	18.0566	17.9775	17.9030	17.8399
	1.00001	18.1065	18.1416	18.1109	18.0201	17.9351
NAC in [2:3] [DMF–H_2O]	0.10002	16.6150	16.5435	16.4850	16.4330	16.4061
	0.30001	16.8059	16.7347	16.6662	16.6046	16.5593
	0.50002	16.9831	16.9123	16.8429	16.7845	16.7336
	0.70002	17.1566	17.0795	17.0081	16.9544	16.9138
	0.90003	17.4823	17.3890	17.2962	17.2197	17.1604
	1.00001	17.6800	17.6279	17.5696	17.4658	17.4346
NAC in [1:4] [DMF–H_2O]	0.10001	15.7269	15.6917	15.6502	15.6201	15.6056
	0.30001	15.8893	15.8388	15.7960	15.7703	15.7575
	0.50001	16.0575	15.9996	15.9590	15.9312	15.9118
	0.70003	16.2686	16.2099	16.1626	16.1358	16.1128
	0.90004	16.4578	16.4024	16.3778	16.3538	16.3272

	1.00001	16.6137	16.5998	16.5485	16.5623	16.5614

It is evident from Table 4.18, 4.19in all cases of NAC–H_2O, NAC–DMF and NAC–DMF–H_2O system, positive value of ΔG increases with the increase in solute concentration and the rise of temperature. This behavior of ΔG [92] suggests that the work is required for viscous flow. Lower values of ΔG at higher temperatures may be due to weaken solute–solvent and solvent–solvent interactions for greater thermal agitation. The positive value of ΔH increases with the increase of solute composition. This indicates that to overcome the energy barrier, some positive work has to be done. Thus the viscous flow is not favored for all the NAC molecules in solution systems. This might be due to the fact that the ground state of the binary and ternary systems is more organized than the transition states.For NAC–DMF system $\Delta S < 0$ and $\Delta H > 0$, the process is never spontaneous, but the reverse process is always spontaneous. In fact, change of enthalpy, ΔH* and change of entropy, ΔS* are derived from viscosity and molar volume as secondary derived data. It can also be here mentioned that the instrumental limitations during the experiments. So some irregularities as well as some ambiguity may be present in change enthalpy, ΔH* and change entropy, ΔS* values.

Table 4.20: Change of Enthalpy, ΔH* and Entropy, ΔS* of N–Acetylcysteine in DMF and water system at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc.(mol/L)	Change of Enthalpy, ΔH* $JK^{-1}mol^{-1}$	Change of Entropy, ΔS* $JK^{-1}mol^{-1}$
NAC–H_2O	0.1001	15010.2419	1.2836
	0.3001	15373.1266	1.8303
	0.5006	15727.9637	2.3671
	0.7003	16354.2948	3.7700
	0.9002	16556.2278	3.6408
	1.0001	16875.5376	4.2642
NAC–DMF	0.1001	7614.7780	-23.9316
	0.3001	8521.3316	-22.7228
	0.5004	9663.3953	-20.2309
	0.7002	9995.6633	-20.4997
	0.9002	10480.5979	-19.8456
	1.001	10476.5889	-20.6003

4.21: Change of Enthalpy, ΔH* and Entropy, ΔS* of NAC in [4:1], [3:2], [2:3] and [1:4] [DMF–H_2O] systems at 298.15 to 318.15 K at 5 K interval

Name of the system	Conc.(mol.L^{-1})	Change of Enthalpy, ΔH* $JK^{-1}mol^{-1}$	Change of Enthalpy, ΔS* $JK^{-1}mol^{-1}$
NAC in [4:1] [DMF–H_2O]	0.10001	18526.3431	5.1167
	0.30021	18118.4682	3.3506
	0.50001	18556.2646	3.9286
	0.70002	19086.8922	4.6940
	0.90001	19452.2558	5.1159
	1.0001	19080.5251	3.2736
NAC in [3:2] [DMF–H_2O]	0.10001	20761.7746	12.0134
	0.30002	21187.8372	12.3853
	0.50012	22799.4386	17.0649
	0.70001	21368.0417	11.5104
	0.90006	21271.7007	10.7397
	1.00001	20865.1183	9.0938
NAC in [2:3] [DMF–H_2O]	0.10002	19771.2515	10.6272
	0.30001	20526.7489	12.5024
	0.50002	20724.3918	12.5689
	0.70002	20804.6144	12.2737
	0.90003	22338.0516	16.3184
	1.00001	21579.8460	13.0595
NAC in [1:4] [DMF–H_2O]	0.10001	17605.0287	6.3155
	0.30001	17876.3232	6.7044
	0.50001	18206.5498	7.2521
	0.70003	18572.8332	7.7719
	0.90004	18304.9958	6.2346
	1.00001	17471.6933	2.9030

CHAPTER V

Conclusion

In order to determining the molecular interactions among NAC, DMF and H_2O volumetric and viscometric investigations have been carried out. Discussing all results and data the following decisions have been taken into account.

(i) Throughout the all investigated systems volumetric, viscometric and thermodynamic properties are depended upon the concentration of NAC as well as on the temperature. The order of density:

NAC– H_2O> NAC in [1:4] [DMF–H_2O] > NAC in [2:3] [DMF–H_2O] > NAC in [3:2] [DMF–H_2O] >NAC in [4:1] [DMF–H_2O] > NAC–DMF

(ii) Apparent Molar Volume decreased with increasing concentration of NAC for all other solutions except NAC–H_2O, NAC in [1:4] and [2:3] [DMF–H_2O] solvent systemsi.e., solute-solute interactions predominant in NAC–H_2O, NAC in [1:4] and [2:3] [DMF–H_2O] solvent systems but in all other systems solute-solvent interactions are predominant.

(iii) Values of apparent molar volume at infinite dilution are positive, which indicates solute-solvent interactions are present in the systems.

(iv) Positive S_v values for NAC–H_2O, NAC in [1:4] and [2:3] [DMF–H_2O] solvent systems predict that solute-solute interactions are predominant as compared to pair-pair interactions.

(v) The negative S_v values for NAC in DMF and NAC in [4:3] and [3:2] [DMF–H_2O] solvent systems predict that ion–solvent interactions prevail as compared to ion–ion interactions.

(vi) In all binary and ternary systems viscosity increased with concentration of NAC but decreased with temperature.

(vii) The ΔG^* and ΔS^* (except NAC–DMF) values are positive for all solutions; i.e., so the process will be non-spontaneous at low temperatures and spontaneous at high temperatures.

(viii) A co-efficients are negative except [4:1] [DMF–H_2O] whereas those of B co-efficients are positive, suggesting weak solute-solute and strong solute-solvent interaction present in the binary and ternary solution.

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