MICELLAR INTERACTIONS OF SDS (SODIUM DODECYL SULFATE) IN AQUEOUS MEDIA CONTAINING BUTYLATED HYDROXY ANISOLE (ANTIOXIDANT)

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Waknaghat

TALBLE OF CONTENTS

CERTIFICATE

This is to certify that the work titled "**Micellar Interactions of SDS (Sodium Dodecyl Sulfate) in aqueous media containing Butylated Hydroxy Anisole(BHA)"** submitted by " **Tanvi Chaudhary and Ishita Sharma**" in partial fulfillment for the award of degree of **B. Pharmacy** of Jaypee University of Information Technology, Waknaghat has been carried out under my supervision. This work has not been submitted partially or wholly to any other University or Institute for the award of this or any other degree or diploma.

Signature of Supervisor .....28/5/12.....

Name of Supervisor Dr. Poonam Sharma

Designation Lecturer

Date 28/5/12

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SUMMARY

Conductivity, viscosity and sound velocity measurements of aqueous solution of the anionic surfactant SDS (sodium dodecyl sulfate) with BHA (butylated hydroxyl anisole) (0.1,0.2 and 0.3 $mM.dm^{-3}$) have been carried out in the different temperature range 25-40 °C. From electrical conductivity measurements, the critical micelle concentrations (CMCs) of SDS has been determined in the above aqueous media with BHA. From the CMC values as a function of temperature, various thermodynamic parameters have been evaluated: the standard enthalpy change (ΔH°_{m}), standard entropy change (ΔS°_{m}), and standard Gibbs energy change (ΔG°_{m}) for micellization.

This work also included viscosity studies of aqueous solutions of SDS with the antioxidant (BHA) in order to determine the viscosity (η).From viscosity data A and B co-efficients were calculated.

From sound velocity measurements, the compressibility coefficient (β), apparent molar volume (Φv) and apparent molar compressibility ($\Phi \kappa$) have been computed.

All of these parameters are discussed in terms of solute-solute and solute-solvent interactions resulting from more of hydrophobic interactions and as well as electrostatic interactions.

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List of Symbols and acronyms

SDS	Sodium dodecyl sulfate
BHA	Butylated Hydroxy Anisole
API	Active Pharmaceutical Ingredient
β	Compressibility Coefficient
Φ_v	Apparent Molar Volume
Φ_k	Apparent Molar Compressibility
ΔH°_m	Standard Enthalpy Change
ΔS°_m	Standard Entropy Change
ΔG°_m	Standard Gibbs Free Energy Change
IBU	Ibuprofen
Γ	Viscous Relaxation time
V_f	Free Volume
π_i	Internal Pressure
MCE	Molar cohesive energy
$\Delta\beta$	Change in Adiabatic Compressibility
$\Delta\beta/\beta_0$	Relative Change in Adiabatic Compressibility
Φ°_K	Limiting Apparent Molal Compressibility
Φ°_V	Limiting Apparent Molal Volume
κ	Specific Conductance
CMC	Critical Micelle Concentration
η	Viscosity co-efficient
η_r	Relative viscosity

INTRODUCTION

1. Introduction

In recent days, drug-surfactant systems constitute one of the most spectacular branches of the modern science that has seen input from many disciplines including chemistry, physics, biochemistry and biotechnology. It is because of the reason that properties of such systems find useful applications in biological, pharmaceutical and industrial systems. However, due to the availability of new experimental techniques and the production of novel surfactant molecules, these studies continue to carry interest for the researchers in academics to provide systematic understanding of the subject.

The knowledge of molecular mechanism of drug-membrane interaction is not only of theoretical significance, but also of potential practical implications [1]. Drug molecules are chemical entities used for the purpose of diagnosis, prevention, treatment, or cure of a disease by altering the physiological system of the body. They are characterized by the presence of different functional groups such as polar (hydrophilic) and non-polar (hydrophobic) groups that are responsible for their therapeutic properties. So, a systematic knowledge of the solution behavior of drug molecules/excipients can be of great significance in understanding their physiological action [2]. Chemically, the drug action can be described as:

Drug (D) + Receptor (R) ⟷ Drug Receptor Complex (DR) ⟹ Response

The interaction between drug and body are conveniently divided into two classes [3]:

(i) **Pharmacodyanamic process** (action of drug on the body)

(ii) **Pharmacokinetic process** (action of the body on the drug)

These above mentioned classes are the ultimate consequences of physicochemical interactions between drug/drug excipients and functionally important molecules in the living organism.

However, excipients (drug additives) are compounds other than active ingredients that are intentionally incorporated into pharmaceutical dosage forms and play specific functional roles in formulation of dosage forms. They can initiate,

propagate or participate in chemical or physical interactions with an active ingredient. The term excipients come from a latin word, *excipere* which means to receive, to gather and to take out. This refers to one of the properties of an excipient which is to ensure that a medicinal product has weight, consistency and volume necessary for correct administration of the active principle [4]. Three essential requirements [5] of active principles are compared with those of excipients.

The requirement of therapeutic efficacy for drugs is replaced by that of functionality for excipients defined as physical, physiochemical and bio-pharmaceutical properties. So excipients can no longer be considered as mere inert supports for the active principles but also essential functional components of a modern pharmaceutical formulation [6] which are given as below:

API+ Excipient + Process+ Interaction = Formulation

1.1 Butylated Hydroxy anisole (BHA): It is an antioxidant consisting of a mixture of two isomeric organic compounds as shown in Figure 1.

2-*tert*-Butyl-4-methoxy-phenol (a)

3-*tert*-Butyl-4-methoxy-phenol (b)

Figure 1. Structural representation of Isomeric form of BHA

The primary use of BHA is an antioxidant [7] and preservative in food packaging, cosmetics et cetera. BHA is also commonly used in medicines such as Isostretinoin,

Lovastatin et cetera. So, due to its properties BHA is considered very important ingredient used as drug excipient.

1.2 Sodium Dodecyl Sulfate (SDS): As the drug molecules find their way into biological systems through membranes. These membranes have lipid bilayered structures which resembles closely with surfactant molecules. Surfactants are amphiphilic molecules consisting of polar (hydrophilic) and non-polar (hydrophobic) parts which are responsible to undergo aggregation [8], i.e., micellization. This micellization or association phenomena occurs as a result of a delicate balance between various repulsive and attractive forces present in their solutions. SDS an anionic surfactant is best known and extensively studied in relation for its micellization, properties and phase behavior whose structure is as shown below:

These surfactant molecules find extensive application in different formulations in drug industry as they can act as wetting agents, solubilizers or emulsifiers. They may enhance the membrane permeability, thus causing the greater absorption of most of the medicines or help in increasing the surface area for absorption. A systematic knowledge of solution behavior of drugs/drug excipients can be of great significance in order to understand their physiological action which can be achieved with the help of transport property measurements. In this regard, conductance, viscosity and ultrasonic velocity methods have been successfully used to access the thermodynamic parameters [9] of various biological molecules. In addition these studies also throw light on solute-solvent interactions which may be helpful for pharmaceutical applications of drugs.

In this project, the transport techniques have been used to reveal the effect of intermolecular interaction [10-11] of BHA (antioxidant) and SDS (surfactant) in aqueous medium.

REVIEW/BACKGROUND MATERIAL

2. Review / Background material

2.1 Review of literature

In the following section, recent published studies on drug-surfactant have been presented, illustrating the involvement of various kinds of interactions which these molecules can undergo. Techniques that are commonly employed for the purpose are spectroscopic and thermodynamic methods.

Pifferi et.al [5] examined the role and safety of pharmaceutical excipients and their importance with respect to API. The most important part of a medicine as far as its weight is concerned, is constituted by its excipients, which have the important functions of guaranteeing the dosage, stability and bioavailability of the active principle. In this article they review the principal classes of excipients and their respective side effects.

Ravichandran S. [10] studied ultrasonic velocity and density in the mixture of cholesterol in ethanol and 1-propanol solution at different concentration to study the thermodynamic properties. Acoustical parameters like adiabatic compressibility, intermolecular free length, acoustic impedance and surface tension are calculated using the ultrasonic velocity and density. These data are particularly discussed with respect to the concentration of cholesterol. The variation of ultrasonic velocity shows a dip at higher concentration of cholesterol. These properties are used to illustrate the nature of interactions between component molecules.

A. Amararene et.al. [11] studied using a custom-built ultrasound velocimeter to carry out high-precision velocity measurements of reverse micelle solutions, made of ionic (AOT) and nonionic ($C_{12}E_4$) surfactants in oil, as a function of water concentration. They showed that the observed velocity variation as a function of increasing water concentration differs from the characteristics of the surfactant polar head groups. The complex profile of compressibility curves obtained from velocity and densimetric measurements can be accounted for by the relation existing between

the surface polar head group of each surfactant and the number of interacting water molecules. At the highest water concentration, the compressibility parameters obtained are different from those reported for "bulk" water and reflect the peculiar properties of confined water.

Chauhan et. al [12] has calculated compressibility coefficient (β), apparent molar volume (Φ_v) and apparent molar compressibility (Φ_k) from sound velocity and density measurements of aqueous solutions of the anionic surfactant SDS (sodium dodecyl sulfate) and the cationic surfactant CTAB (cetyltrimethylammoniumbromide) with the drug furosemide (0.002 and 0.02 $mol \cdot dm^{-3}$) in the temperature range 20°C – 40°C. The critical micelle concentrations (CMCs) of SDS and CTAB in the above aqueous furosemide solutions were determined from electrical conductivity measurements. From the CMC values as a function of temperature, they have evaluated various thermodynamic parameters: the standard enthalpy change (ΔH°_m), standard entropy change (ΔS°_m), and standard Gibbs free energy change (ΔG°_m) for micellization. Viscosity as well as UV- Visible studies of aqueous solutions of SDS and CTAB in presence of drug have also been carried out to interpret all these parameters in terms of drug-drug, drug-solvent and drug-surfactant interactions resulting from of various electrostatic and hydrophobic interactions.

Dubey [13] studied the CMC of SDS in dilute aqueous solutions of 1-propanol, 1-butanol, 1-pentanol and 1-hexanol at 298, 303, 308 and 313K. Thermodynamic parameters of micellization as enthalpy (ΔH°_m), entropy (ΔS°_m) and free energy (ΔG°_m) were calculated from temperature dependence of CMC. The dependence of these thermodynamic parameters on the concentration of alcohols was determined in terms of the effect of additives as well as that of chain length of alcohols.

Patrick J. Crowley et.al [14] studied the drug excipient interactions. Although considered pharmacologically inert, excipients can initiate, propagate or participate in chemical or physical interactions with drug compounds, which may compromise the effectiveness of a medication.

M. Jahirul Islam et.al [15] studied the effect of some biologically important compounds such as calcium chloride, calcium fluoride, calcium oxalate and calcium acetate as well as some alpha-amino acids on the micellar properties of an anionic surfactant, SDS with the help of conductance measurement techniques.

Mishra et.al [16] reviewed the potential applications of surfactants. Surfactants play a vital role in various drug deliveries. To formulate compounds sparingly soluble in water, pharmaceutically acceptable co-solvents or surfactants are typically employed to increase solubility by explaining the mechanism to form micelles and its applications related to various site of action.

C. O. Rangel-Yagui et.al [17] studied the solubilisation of ibuprofen (IBU) in micellar solutions of three surfactants possessing same hydrocarbon tail but different hydrophilic head groups as SDS, DTAB and $C_{12}EO_8$. The results showed that, irrespective of surfactant type, the stability of IBU increased linearly with increasing surfactant concentration, as a consequence of the association between drug and the micelles.

Brime et. al [18] successfully entrapped amphotericin B in lecithin based microemulsions which is otherwise difficult to deliver due to its insolubility in water as well as oils and shows several adverse effects. Authors evaluated the toxicity of these emulsions in mice in comparision to the marketed formulation. Acute toxicity studies indicated that the mortality rate of amphotericin B microemulsions was lesser than that of mixed micellar formulation. In other investigation, same authors [19] evaluated that there was three fold increases in the tolerated dose of amphotericin when it was administered as microemulsion in the immunocompetent and neutropenic mice infected with systemic candidacies, as compared to that of marketed formulation. Further, they came to know that the microemulsions were superior to marketed formulation with respect to ability to reduce fungal load and to increase the survival period of the mice.

Sharma et.al [20] measured the viscosity and ultrasonic velocity of narcotic analgesic drugs in aqueous mixtures of methanol, ethanol and1-proponal. Various acoustical parameters have been obtained which include viscous relaxation time (Γ), free volume (V_f), internal pressure (π_i) and molar cohesive energy (MCE). The dependence of these properties on solvent composition is found to originate from hydrophobic hydration phenomenon. In other investigation, same authors [21] further extended studies for solutes like electrolyte sodium chloride, surfactant: sodium dodecyl sulfate and non-electrolyte sucrose in presence of narcotic analgesic drugs. The viscosity data have been analyzed for the evaluation of A and B coefficient. It can be inferred from these studies that all the drug cations can be structure makers/promoters due to hydrophobic hydration of drug molecules. Furthermore, the results are correlated to understand the solution behavior of drugs in aqueous alcoholic solutions as a function of the nature of alcohols and different type of solutes.

Mehta et. al [22] studied the behavior of Rifampicin (D) with b-cyclodextrin (b-CyD) in aqueous media (D) by means of UV-visible spectroscopy and conductivity measurements over the temperature range 15-30°C. The UV-visible study has been used to characterize the systems. However, the conductivity was measured (i) as a function of (D) for binary D/W system (ii) as a function of (CyD), keeping the concentration of the drug constant for D/CyD/ W (iii) as a function of (D)in the presence of a constant CyD concentration. The stoichiometry of the association was estimated from conductivity data at which the change in slope of κ occurs. The standard free energy change ΔG°_{m} of aggregation was also interpreted in terms of stoichiometry of β-cyclodextrin: rifampicin association.

Rita Mehra et.al.[23] studied sound speed, density and viscosity of glycine in aqueous galactose solution at varying concentrations from 0.1035 to 1.0345 m at 298, 308 and 318 K have been determined. Density, viscosity and sound speed have been measured by using pre-calibrated bicapillary pycnometer, Ostwald's viscometer and single-frequency ultrasonic interferometer at 2 MHz frequency, respectively. The derived acoustic parameters like free volume(V_f), adiabatic compressibility (β), hydration number (n_H) and Gibbs free energy for activation (ΔG), acoustic impedance (Z), intermolecular free length (L_f) and relative association (R_A), internal pressure

(π_i) , Rao's constant (R), Wada's constant (W) have been calculated from experimental data. All the measurements have been carried out in a thermostatic water bath having PT-100 sensor with circulating medium with an accuracy of ± 0.1°C. Solute-solvent interactions dominate over solute–solute interactions and, the solute-solvent interactions increase with temperature.

R.Ezhil Pavai et al. [24] studied density, viscosity and ultrasonic velocity of L-threonine in aqueous potassium nitrate (0.04, 0.06 and 0.08M) solutions have been measured as a function of concentration of amino acid and electrolyte at 303 K. Experimental data have been used to estimate the adiabatic compressibility (β), change in adiabatic compressibility (Δβ), relative change in adiabatic compressibility ($\Delta\beta/\beta_0$), apparent molal compressibility (Φ_K), apparent molal volume (Φv), limiting apparent molal compressibility (Φ°_K), limiting apparent molal volume (Φ°_V) and their constants (S_k, S_v) and viscosity B-coefficient. These parameters have been interpreted in terms of ion-ion and ion-solvent interactions.

2.2 Aim of Present work

Drug-surfactant interaction is an important and inevitable bio-physical and chemical phenomenon. Drug actions i.e. drug reaching the blood stream, its extent of distribution, its binding to the receptors and finally producing the physiological action, all depend on various physicochemical properties chiefly decided by various interactions e.g. ionic, covalent, charge transfer, hydrogen bonding or hydrophobic interactions etc. Transport property measurements are a powerful tool to study the behavior of various solutes/drugs in solutions. The most important part of a medicine as far as its weight is concerned is constituted by its excipients, which have important functions of guaranteeing the dosage, stability and bioavailability of the active principle. Excipients constitute the mass or greater volume in the usual enternal or parenteral formulations which often contain reactive functional groups that may give rise to chemical or physical transformations. These excipients molecules find their way into biological systems through membranes which have lipid bilayered structures that closely resembles with surfactant molecules.

The objective of present project is to understand the drug excipient-surfactant interaction using different experimental conditions such as temperature. The emphasis is laid on hydrophobic and electrostatic interactions which exist both in drug excipients (BHA) and surfactant (SDS). However, a detailed survey of literature reveals that solution behavior of BHA +SDS continues to interest the researchers in academics; primary for the reason that both BHA and SDS have polar as well as non polar parts and their interactions is not completely understood as yet on many accounts. In the present work, therefore attempts have been made to investigate the solutions behavior of BHA-SDS (antioxidant-surfactant) interactions in aqueous media by volumetric and thermodynamic methods. These interactions can occur either at interface or the interior of these highly aggregated or micelles which are further applied in drug delivery in order to minimize drug degradation and loss, to prevent harmful side effects and to increase drug bioavailability.

METHODOLOGY

3. Methodology

3.1 Thermostat and temperature control

All the measurements were carried out in an automatic digital temperature controller high precision water thermostat (HARCO) having a temperature control of accuracy ±0.05 °C.

3.2 Conductance measurements

Conductance measurements were carried out with a calibrated digital conductivity meter (Cyber Scan CON 510 supplied by Merck). Specific conductance (κ) have been measured at four different temperature i.e. 25°C, 30°C, 35°C and 40°C by varying the concentration of SDS (1mM dm^{-3} to 14mM dm^{-3}) at 0.001 $mol.dm^{-3}$, 0.002 $mol.dm^{-3}$ and 0.003 $mol.dm^{-3}$ concentrations of BHA. From the graphs of κ vs concentration of SDS, CMC were evaluated and different thermodynamic parameters standard enthalpy change (ΔH°_{m}), standard entropy change (ΔS°_{m}), and standard Gibbs energy change (ΔG°_{m}) were also calculated.

3.3 Viscosity measurements

Viscosity measurements were carried out with a calibrated jacketed Ubbelhode Viscometer. The precision achieved in viscosity measurement was ±0.01%.Density measurements were carried out with the help of specific gravity bottle. The viscosities and densities of aqueous solutions of BHA and SDS were measured at different temperatures i.e 25°C, 30°C, 35°C and 40°C. From viscosity data A and B coefficients were calculated with the help of Jones Dole equation which are interpreted in terms of solute-solute and solute-solvent interactions.

3.4 Ultrasonic Sound Velocity

Ultrasonic velocities were measured by using Ultrasonic Interferometer (Mittal M-81) for the same concentration range of SDS and BHA. Various acoustical parameters were calculated such as the compressibility coefficient (β), apparent molar volume (Φ_v) and apparent molar compressibility (Φ_k). Propagation of Ultrasonic waves being sensitive to the nature of the solvent medium, contributes to understand different kind of interactions that drug/surfactant molecules undergo in solution.

RESULTS & DISCUSSIONS

4. Results and Discussion

4.1 Conductivity Studies:

The micellization behaviour of SDS has been traced for drug excipient-surfactant interactions. The dependence of κ on the concentration of the surfactants (SDS) in aqueous media containing BHA is presented in Figure 2, Figure 3 and Figure 4.The break points were quite significant, therefore allowing CMC (critical micelle concentration) to be evaluated and are reported in Table 1. The CMC values of SDS were found to be in range of (5.8 $mM.dm^{-3}$ to 7.1 $mM.dm^{-3}$) which are lower than its standard value (i.e. $8mM.dm^{-3}$).This indicates that presence of bulkier moiety as *t*-butyl substitution at position 2 and hydroxy group at position 1 played significant role for interaction as proposed in Figure 5. Thus, these substitutions contribute to better interactions leading to micellization much earlier.

This is also due to lowering of repulsion between surfactant head group and also hydrophobic nature of drug which provides surface for micellization of SDS. Hence, the extra hydrophobicity offered by BHA seems to reduce the CMC values.

4.1.1 Thermodynamics of Micellization of SDS in aqueous solutions of BHA

In order to derive further information about antioxidant-surfactant interactions from this experimental data, various thermodynamic parameters of micellization have been calculated and examined. The standard Gibbs free energy [10] change for micellization is given by :

$$\Delta G^{o}_{m} = RT \ln(X_{CMC})$$

where the mole fraction at which the CMC occurs is X_{CMC} = {CMC of surfactant/(CMC of surfactant + concentration of drug + 55.6)} with concentrations in units of $mol \cdot dm^{-3}$, R is the gas constant, and T is temperature in Kelvin. The standard enthalpy change for micellization, $\Delta H°_m$ is obtained through a classical Van't Hoff equation [12] :

$$\Delta H°_m = -RT^2[d \ln(X_{CMC})/dT]$$

where $d \ln(X_{CMC})/dT$ is the slope of the straight line obtained by plotting $\ln X_{CMC}$ against T.

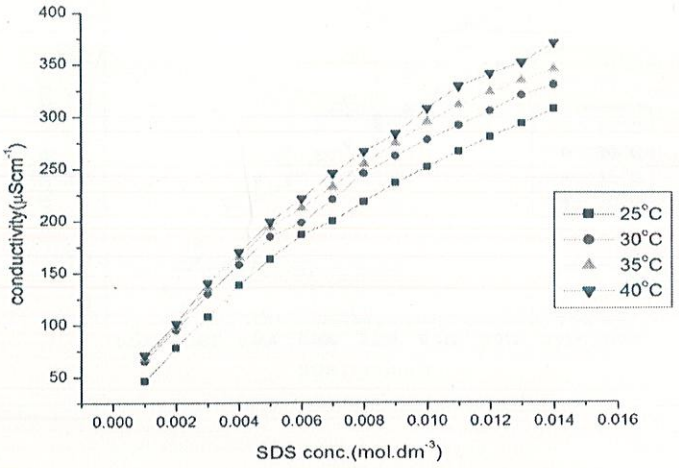

Figure 2. Variation of specific conductance (κ) with concentration of SDS at different temperature in 0.001 mol.dm^{-3} aqueous solution of BHA.

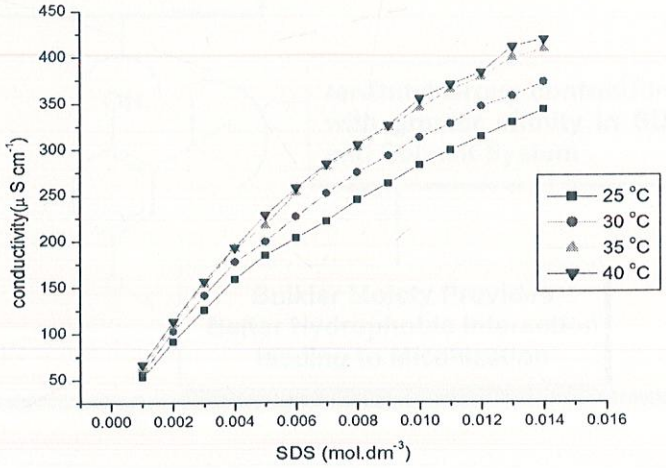

Figure 3. Variation of specific conductance (κ) with concentration of SDS at different temperature in 0.002 mol dm^{-3} aqueous solution of BHA.

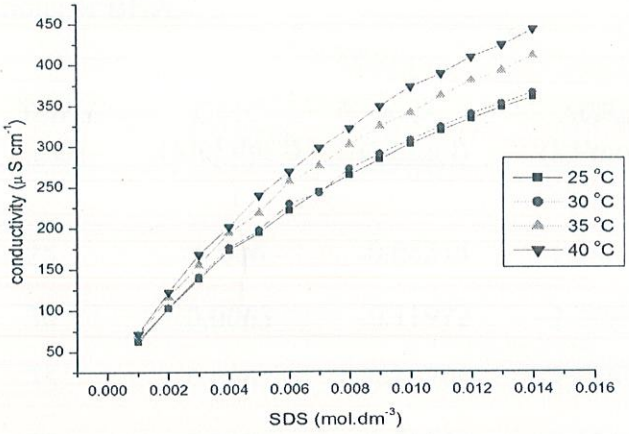

Figure 4. Variation of specific conductance (κ) with concentration of SDS at different temperature in 0.003 mol dm^{-3} aqueous solution of BHA.

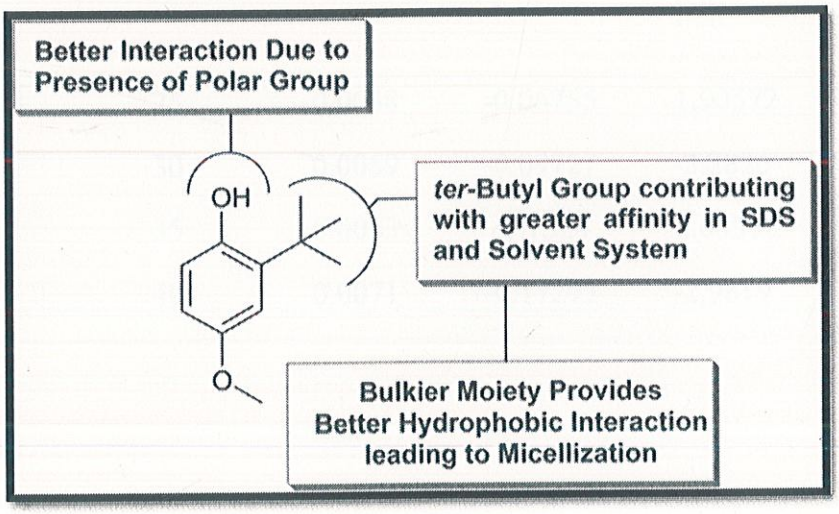

Figure 5. Structural Representation of different substitutions of BHA

Table1. CMC, $\Delta H°_m$, $\Delta G°_m$ and $\Delta S°_m$ values at temperature range (25-40°C) at different concentrations of BHA.

Concentration ($Mol.dm^{-3}$)	Temp. (°C)	CMC ($Mol.dm^{-3}$)	$\Delta H°_m$ (kJ/mol)	$\Delta G°_m$ (kJ/mol)	$\Delta S°_m$ (kJ/mol K^{-1})
0.001	25	0.006	-0.08314	-1.89849	0.072614
	30	0.0063	-0.11972	-2.26602	0.071543
	35	0.0067	-0.16295	-2.62577	0.070366
	40	0.0077	-0.21284	-2.95445	0.06854
0.002	25	0.0058	-0.07275	-1.90564	0.073316
	30	0.006	-0.10476	-2.27832	0.072452
	35	0.0061	-0.14259	-2.65323	0.071733
	40	0.0074	-0.18623	-2.96802	0.069545
0.003	25	0.0058	-0.06755	-1.90572	0.073527
	30	0.0059	-0.09727	-2.2826	0.072844
	35	0.0063	-0.1324	-2.64395	0.071758
	40	0.0071	-0.17293	-2.9819	0.070224

The standard entropy [12] changes for micellization ΔS^{o}_{m} for SDS were determined as-

$$\Delta G^{\circ}_{m} = \Delta H^{\circ}_{m} - T\,\Delta S^{\circ}_{m}$$

The negative magnitude of ΔH^{o}_{m} and ΔG^{o}_{m} and positive magnitude of ΔS^{o}_{m} (Table 1) are indicative of drug excipient-surfactant interactions. Figure 6(a), (b) and (c) illustrate the dependence of these thermodynamic parameters on temperature. However with the increase in concentration of BHA all the parameters almost remain same (Table 1). The decrease in these parametric values with the increase in temperature reflects the decrease of hydrophilic hydration of the surfactant head group as well as the hydrophilic part of BHA, which facilitates the hydrophobic interaction with anionic surfactant SDS thus favoring micellization.

Negative values of ΔH^{o}_{m} showed that the process of solublization of BHA and the interaction with solution of SDS is an exothermic process. However in aqueous medium, solvent polar groups are hydrated and the intermolecular aggregation of drug molecules through their hydrophobic parts is analogous to micellization thus favoring limited aqueous solublization.

The positive ΔS°_{m} values are attributed to the disruption of water structure [13] around hydrocarbon part of these additive molecules BHA/SDS as they transfer from aqueous bulk phase to other parts of micellar aggregates. At the same time, water-water bonds are broken, which in turn increase the randomness of the hydrocarbon chains in micellar core [22, 23]. Thus, the decrease in CMC on addition with BHA may be seen in terms of establishment of additional hydrophobic interactions between the hydrophobic part of SDS and BHA. Also, positive ΔS°_{m} values indicates that system is entropy driven which is due to re-organisation of water molecules.

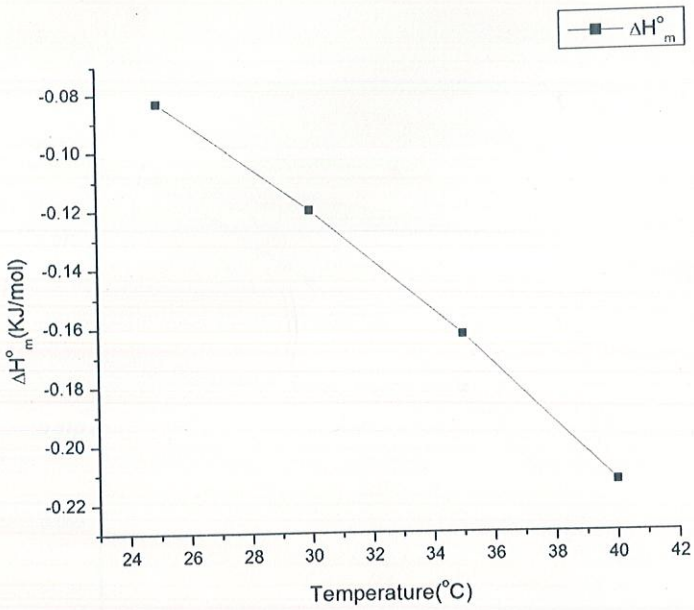

Figure 6(a). Variation of the thermodynamic parameters $\Delta H°_m$ of SDS as a function of temperature in 0.001 mol.dm^{-3} aqueous solutions of BHA.

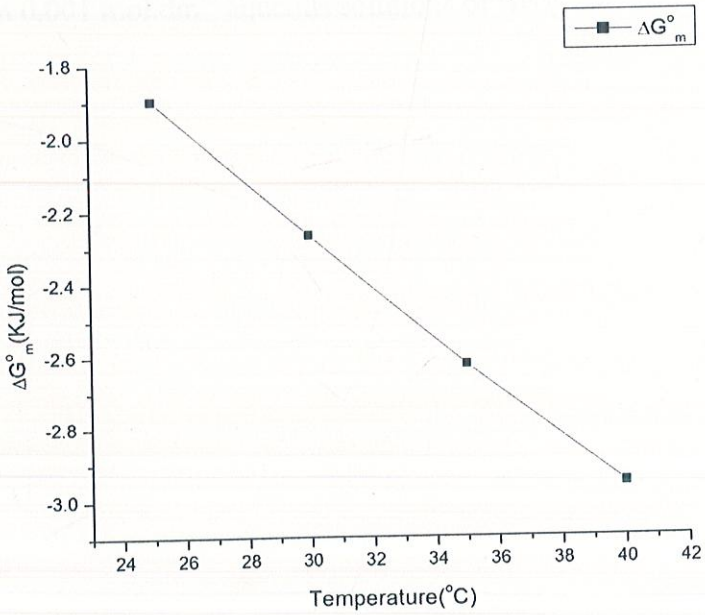

Figure 6(b). Variation of the thermodynamic parameters $\Delta G°_m$ of SDS as a function of temperature in 0.001 mol.dm^{-3} aqueous solutions of BHA.

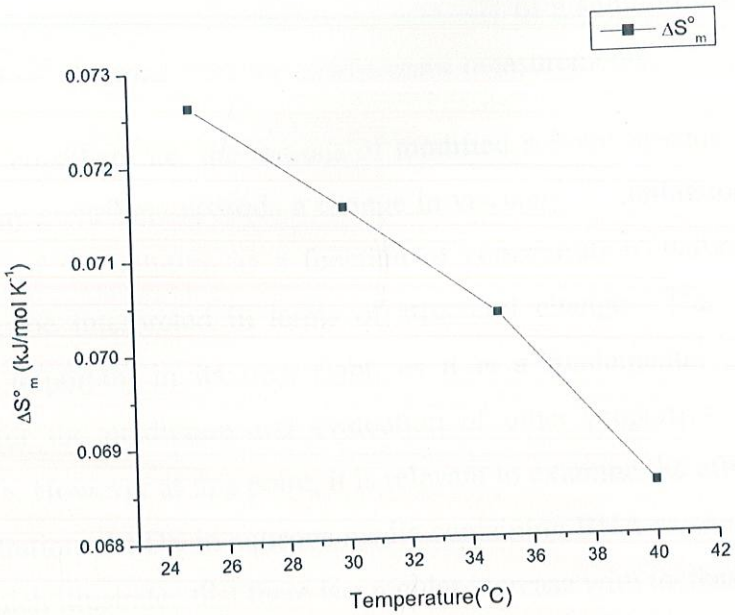

Figure 6(c). Variation of the thermodynamic parameters ΔS°_{m} of SDS as a function of temperature in 0.001 mol.dm^{-3} aqueous solutions of BHA.

4.2 Viscosity Studies :

Information with respect of the solution behavior of drug molecules is obtained from the contribution of drug molecules to the viscosity of a solution which also supports the observations obtained from the conductance measurements.

The co-sphere i.e. the regions of modified solvent system surrounding drug molecule may contribute towards a change in viscosity. Examination of the behavior of viscosity of the solution as a function of concentration, nature of drug/solvent system may be interpreted in terms of structural changes. The viscosity of drug solution is important in its own right, as it is a fundamental transport property necessary for the prediction and evaluation of other properties such as electrical conductance. However at this point, it is relevant to examine the effect of viscosity on the concentration of SDS in aqueous media containing BHA as shown in Figure 7 (a, b and c) which illustrates that there is a regular increase with increase in concentration of SDS. With increase in temperature, decrease in viscosity was observed from 25°C to 40°C with interval of 5°C. A considerable change in the values indicated the temperature dependence. Similar observations are noticed at other concentration of BHA with SDS i.e. 0.002 and 0.003 $mol.dm^{-3}$. All the viscosity data have been summarized in Appendix-I

From viscosity data A and B coefficients [19] were calculated with the help of Jones Dole equation as and are reported in Table 2 :

$$\eta_r = \eta/\eta_o = 1 + AC^{1/2} + BC \quad \text{or}$$

$$(\eta_r - 1)/C^{1/2} = \Psi = A + BC^{1/2}$$

where $\eta_r = (\eta/\eta_o)$, and η and η_o are viscosities of solution and solvent system respectively, C is the molar concentration. In this equation, A signifies solute-solute interaction. However, B accounts for the contribution arising from the size of solute, molar volume of the solvent in addition to the contribution due to solute-solvent interactions and estimates the order or disorder introduced by the addition of solute into solvent.

The values of A were negative where as B-coefficient were found to be positive. Since A is a measure of ionic interaction, it is evident that there is a weak

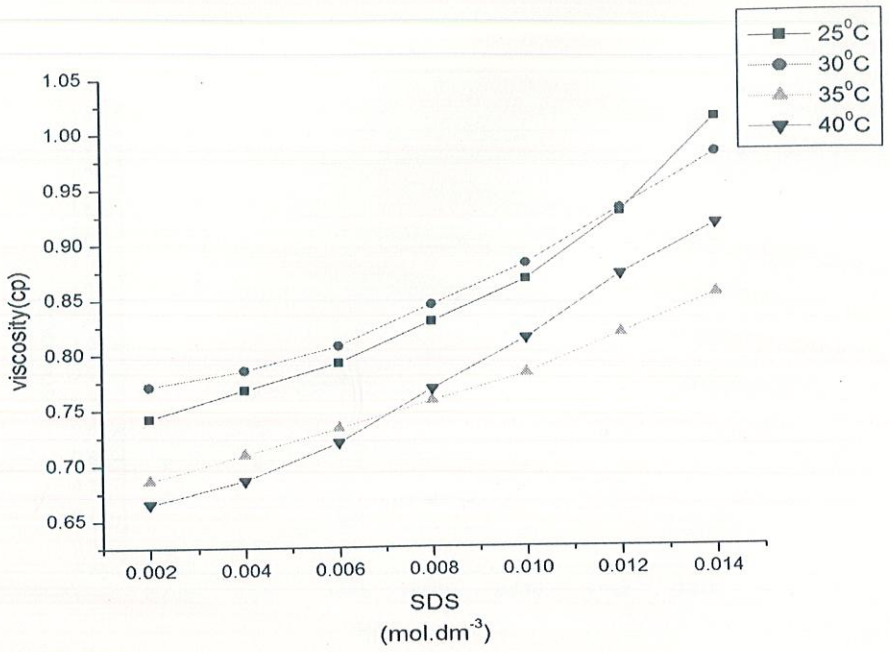

Figure 7(a). Viscosity coefficient (η) as a function of SDS in 0.001 mol.dm^{-3} BHA at different temperatures.

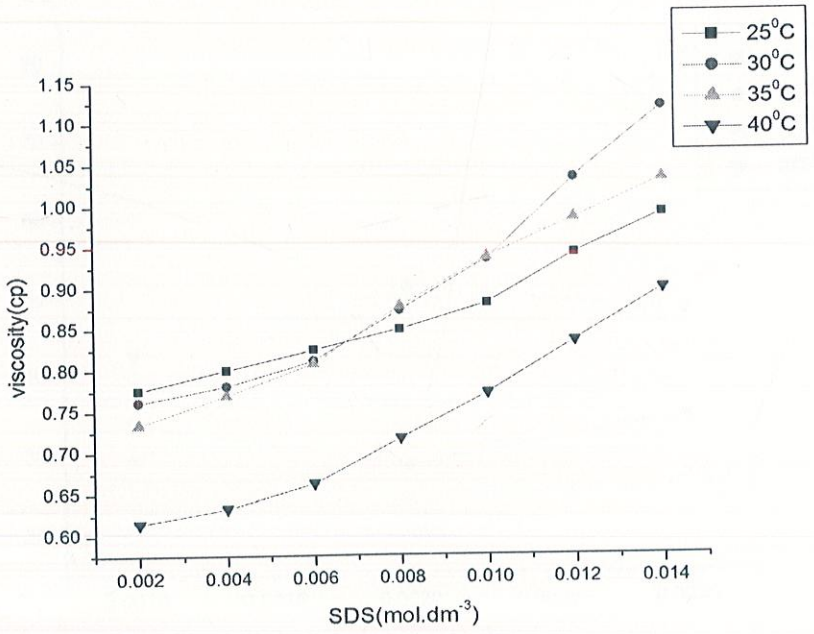

Figure 7(b). Viscosity coefficient (η) as a function of SDS in 0.002 mol.dm^{-3} BHA at different temperatures.

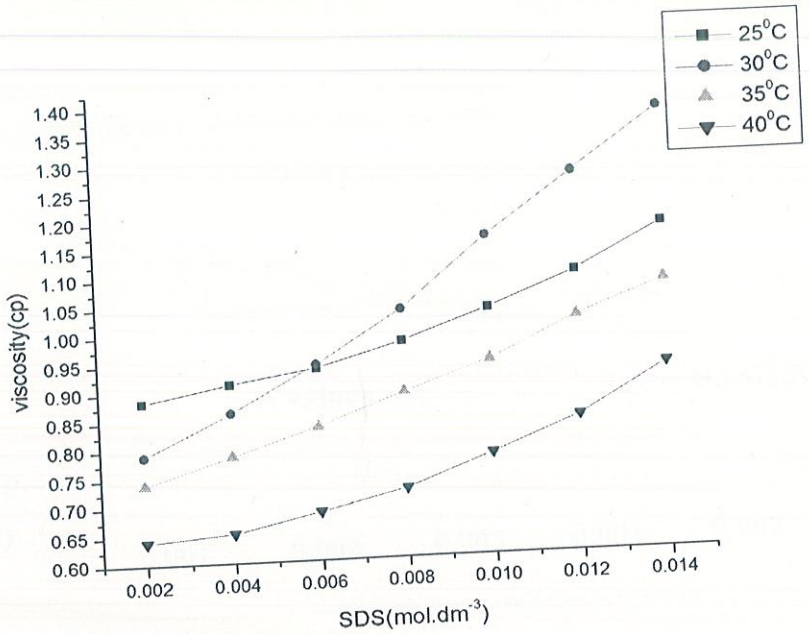

Figure 7(c). Viscosity coefficient (η) as a function of SDS in 0.003 mol.dm^{-3} BHA at different temperatures.

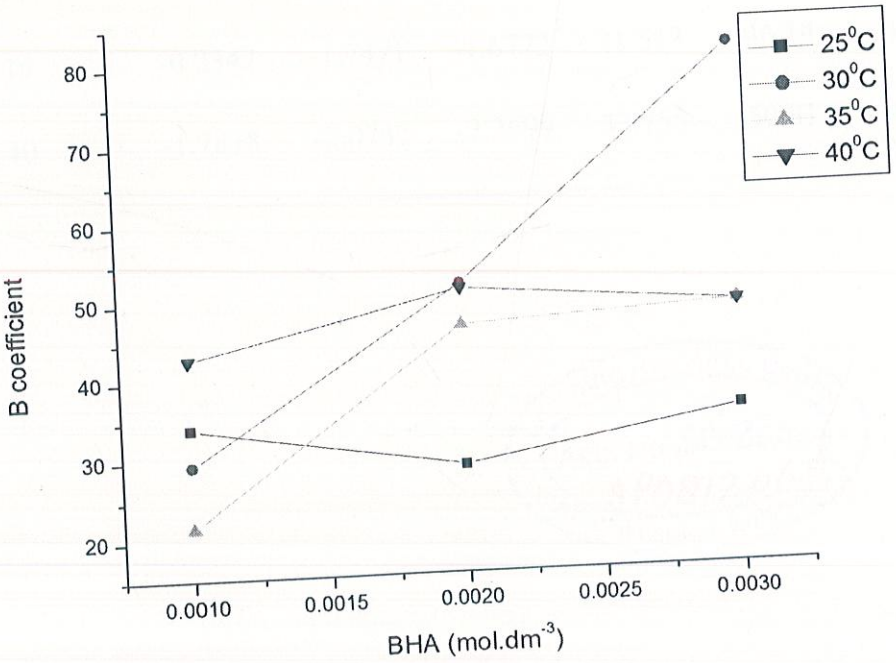

Figure 8. B coefficient as function of BHA at different temperature.

Table 2. A and B coefficients in aqueous solution of 0.001 mol.dm^3, 0.002 mol.dm^{-3} and 0.003 mol.dm^{-3} BHA at different temperatures.

	A values			B values		
Temp. (°C)	**0.001**	**0.002**	**0.003**	**0.001**	**0.002**	**0.003**
25	-0.998	-1.1267	-1.5789	33.927	28.43	34.727
30	-1.2062	-2.2708	-2.6161	29.272	51.42	80.724
35	-0.2342	-1.7471	-1.6772	21.513	46.14	48.129
40	-1.7878	-2.0747	-2.2699	42.755	50.81	48.083

ion-ion interaction, which is indicated by the smaller magnitude of A values. B-coefficient is known as a measure of solute-solvent interaction and is directly dependent on the size, shape and charge of the solute molecules. Thus, B values reflect the net structural effects of the solute and solvent molecules. The positive behaviour of B-coefficient suggests the existence of strong solute-solvent interaction and temperature dependent changes as shown in Figure 8.

4.3 Ultrasonic Sound Velocity Studies :

Ultrasonic velocity in combination with density & viscosity furnish information that takes into account the contributions arising from different kinds of interactions with respect to behaviour of solute spaces in solution. In view of these experimental facts it is intended to undertake ultrasonic sound velocity measurements of SDS in aqueous solution of BHA. All the ultrasonic sound velocity and density data are reported in Appendix-I.

From the measured density and sound velocity values, different parameters such as the apparent molar volume (Φ_v), apparent molar compressibility (Φ_k) and compressibility coefficient (β) [24-28] were evaluated using the following relations and reported in Tables 3-6:

(i) Compressibility coefficient (β): -

$$\beta = 1/dv^2$$

where d is density and v is ultrasonic velocity of solution.

(ii) Apparent molar volume Φ_v ($m^3\ mol^{-1}$) :-

$$\Phi_v = 1000(d_o\text{-}d) / mdd_o + M / d$$

where m is the molality, d_o density of pure solvent, d is the density of solution and M is the relative molar mass.

(iii) Apparent molar compressibility:-

$$\Phi_k = 1000(\beta - \beta_o) / mdo + \Phi_v \beta$$

where $\beta = 1/dv^2$ and $\beta_o = 1/d_o v^2_o$ refer to the adiabatic compressibility coefficients of solution and solvent respectively.

Consistent decrease was found with increase in temperature for β values ranging from 25-40 °C with interval of 5 °C. With increase in concentration of BHA, a decrease in β values were noticed (0.001 $mol.dm^{-3}$, 0.002 $mol.dm^{-3}$and 0.003 $mol.dm^{-3}$) as shown in Figure 9. Decrease in the β values is indicative of interactions with more efforts to compress the system. Significant interactions were accounted with interactive BHA and SDS due to extra hydrophobic hydration which is found to be temperature dependent [26, 29].

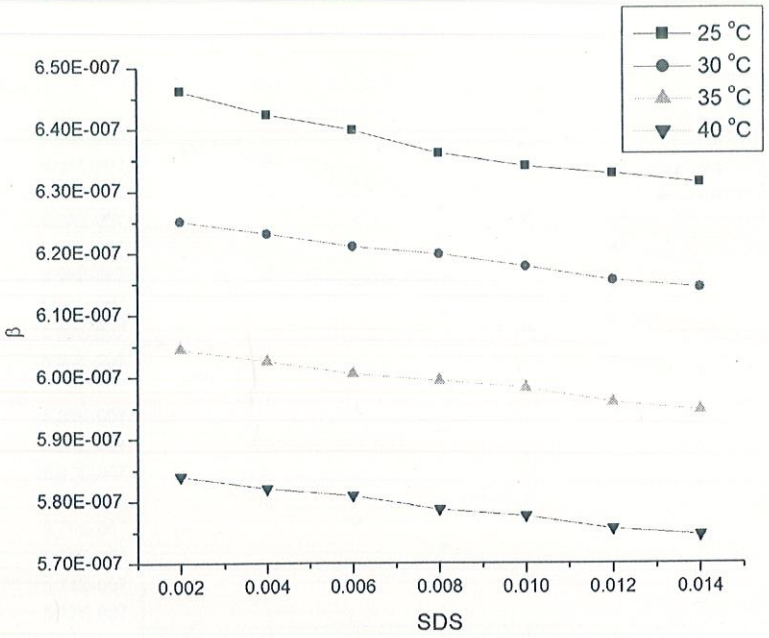

Figure 9(a). Adiabatic compressibility (β, atm^{-1}) co-efficient as a function of SDS in 0.001mol.dm^{-3} BHA at different temperatures.

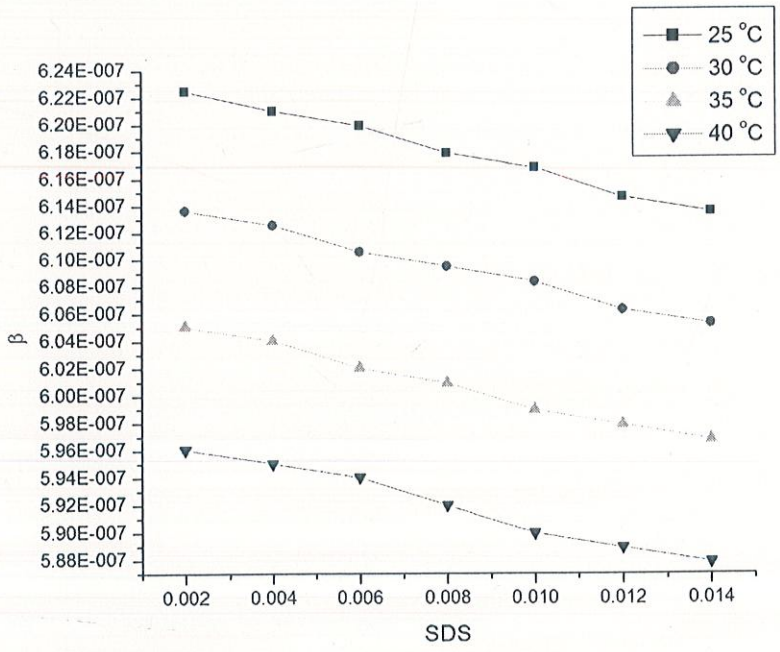

Figure 9(b). Adiabatic compressibility (β, atm^{-1}) co-efficient as a function of SDS in 0.002 mol.dm^{-3} BHA at different temperatures.

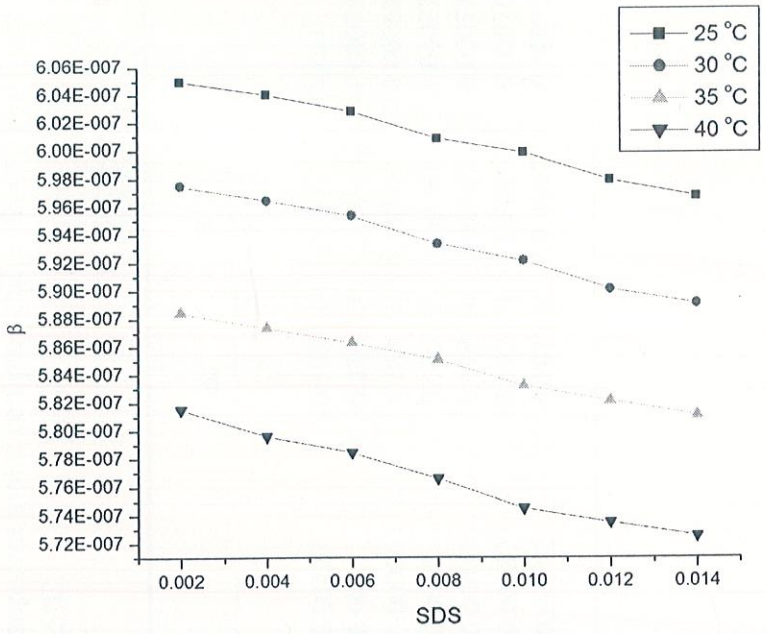

Figure 9(c). Adiabatic compressibility (β, atm^{-1}) co-efficient as a function of SDS in 0.003mol.dm^{-3} BHA at different temperatures.

Table 3. Apparent molar volume Φ_v (m^3/mol), Compressibility coefficient β (atm^{-1}) and apparent molar compressibility Φ_k (m^3 mol^{-1} atm), of SDS in aqueous solution of 0.001 mol.dm^{-3}, 0.002 mol.dm^{-3} and 0.003 mol.dm^{-3} BHA at 25°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k
0.002	-1.34047	6.46E-07	-0.00192	0.188572	6.22E-07	-0.00127	0.188819	6.05E-07	-0.001
0.004	-1.20974	6.42E-07	-0.00193	0.037789	6.21E-07	-0.001	0.239353	6.04E-07	-0.00074
0.006	-0.82789	6.40E-07	-0.00171	0.087982	6.20E-07	-0.00085	0.188743	6.03E-07	-0.00069
0.008	-0.70004	6.36E-07	-0.00176	0.113059	6.18E-07	-0.0009	0.188705	6.01E-07	-0.00077
0.01	-0.66346	6.34E-07	-0.00162	0.138141	6.17E-07	-0.00082	0.198786	6.00E-07	-0.00071
0.012	-0.5299	6.33E-07	-0.00145	0.129725	6.15E-07	-0.00087	0.197063	5.98E-07	-0.00076
0.014	-0.45608	6.31E-07	-0.00134	0.138058	6.14E-07	-0.00082	0.181363	5.97E-07	-0.00073

Table 4. Apparent molar volume Φ_v (m^3/mol), Compressibility coefficient $\beta(atm^{-1})$ and apparent molar compressibility Φ_k (m^3 mol^{-1} atm), of SDS in aqueous solution of 0.001 mol.dm^{-3}, 0.002 mol.dm^{-3} and 0.003 mol.dm^{-3} BHA at 30°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k
0.002	0.290325	6.25E-07	-0.00042	0.188695	6.14E-07	-0.00068	0.188942	5.97E-07	-0.00076
0.004	0.26496	6.23E-07	-0.00072	0.188658	6.13E-07	-0.00061	0.188904	5.96E-07	-0.00064
0.006	0.239576	6.21E-07	-0.00083	0.18862	6.11E-07	-0.00075	0.171964	5.95E-07	-0.00061
0.008	0.201499	6.20E-07	-0.00078	0.188582	6.09E-07	-0.0007	0.163472	5.93E-07	-0.00071
0.01	0.209074	6.18E-07	-0.00082	0.178456	6.08E-07	-0.00067	0.138085	5.92E-07	-0.00069
0.012	0.188744	6.16E-07	-0.00087	0.171691	6.06E-07	-0.00073	0.138043	5.90E-07	-0.00074
0.014	0.181458	6.15E-07	-0.00083	0.18126	6.05E-07	-0.0007	0.145242	5.89E-07	-0.00071

Table 5. Apparent molar volume Φ_v (m^3/mol), Compressibility coefficient $\beta(atm^{-1})$ and apparent molar compressibility Φ_k (m^3 mol^{-1} atm), of SDS in aqueous solution of 0.001 mol.dm^{-3}, 0.002 mol.dm^{-3} and 0.003 mol.dm^{-3} BHA at 35°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k
0.002	0.188881	6.04E-07	-0.00076	0.188828	6.05E-07	-0.00047	0.239929	5.88E-07	-0.00079
0.004	0.188843	6.03E-07	-0.00088	0.18879	6.04E-07	-0.0005	0.189036	5.87E-07	-0.00067
0.006	0.188805	6.01E-07	-0.00092	0.188752	6.02E-07	-0.00067	0.172044	5.86E-07	-0.00062
0.008	0.176105	5.99E-07	-0.00083	0.176068	6.01E-07	-0.00064	0.138105	5.85E-07	-0.00062
0.01	0.148217	5.98E-07	-0.00079	0.178557	5.99E-07	-0.00071	0.148231	5.83E-07	-0.00069
0.012	0.112757	5.96E-07	-0.00084	0.180204	5.98E-07	-0.00068	0.146495	5.82E-07	-0.00066
0.014	0.094661	5.95E-07	-0.00082	0.166914	5.97E-07	-0.00067	0.145242	5.81E-07	-0.00064

Table 6. Apparent molar volume Φ_v (m^3/mol), Compressibility coefficient β(atm^{-1}) and apparent molar compressibility Φ_k (m^3 mol^{-1} atm), of SDS in aqueous solution of 0.001 mol.dm^{-3}, 0.002 mol.dm^{-3} and 0.003 mol.dm^{-3} BHA at 40°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k	ϕ_v	β	ϕ_k
0.002	0.289917	5.84E-07	-0.00099	0.239757	5.96E-07	-0.00097	0.240292	5.82E-07	-0.00023
0.004	0.188772	5.82E-07	-0.001	0.214343	5.95E-07	-0.00075	0.189204	5.80E-07	-0.00061
0.006	0.138189	5.81E-07	-0.00086	0.205846	5.94E-07	-0.00067	0.138119	5.78E-07	-0.0006
0.008	0.087639	5.79E-07	-0.00092	0.176187	5.92E-07	-0.00076	0.150836	5.77E-07	-0.00069
0.01	0.0977	5.78E-07	-0.00084	0.16853	5.90E-07	-0.00081	0.117628	5.74E-07	-0.00076
0.012	0.079158	5.76E-07	-0.00088	0.171875	5.89E-07	-0.00076	0.12949	5.73E-07	-0.00072
0.014	0.094742	5.75E-07	-0.00082	0.166998	5.88E-07	-0.00073	0.137952	5.73E-07	-0.00068

Further insight into the type and extent of interactions of SDS in aqueous media containing BHA is obtained from the behavior of apparent molar volume Φ_v and apparent molar compressibility Φ_k [30, 31]. However, an attempt is made to derive information as regard to drug-surfactant interactions from dependence of Φ_v on the surfactant's concentrations as shown in Figure 10 (a, b and c).

Initial negative values of Φ_v suggested the occurrence of hydrophobic interaction and moreover non-linearity was observed with increase in concentration and temperature. Dominance of hydrophobic interactions facilitates the process of micellization of SDS. Interestingly, it was found that with rise in temperature values of Φ_v become positive indicating that electrostatic interactions are dominating at higher temperature i.e. $\leq$ 30°C. Succinctly, at 25°C (0.001 mol.dm^{-3}) Φ_v was found to facilitate hydrophobic interaction as in support of negative values of Φ_v. Moreover surprisingly with change in concentration of BHA, the values of Φ_v afterward 0.001 mol.dm^{-3} at 30°C, 35°C and 40°C were found positive [12]. This contribution in positive magnitude suggested the observable occurrence of strong electrostatic interactions.

Further the results for Φ_k as shown in Figure 11(a, b and c) represented the dependence of Φ_k as a function of concentration and temperature. With increase in concentration of SDS and temperature decrease in negative values was found. Interestingly the decrease was observed from 25-30°C but a slight consistency was observed at 30°C, 35°C and 40°C at a concentration of 0.001mol.dm^{-3}. Negative magnitude is indicative of strong hydrophobic interactions of BHA facilitated by SDS.

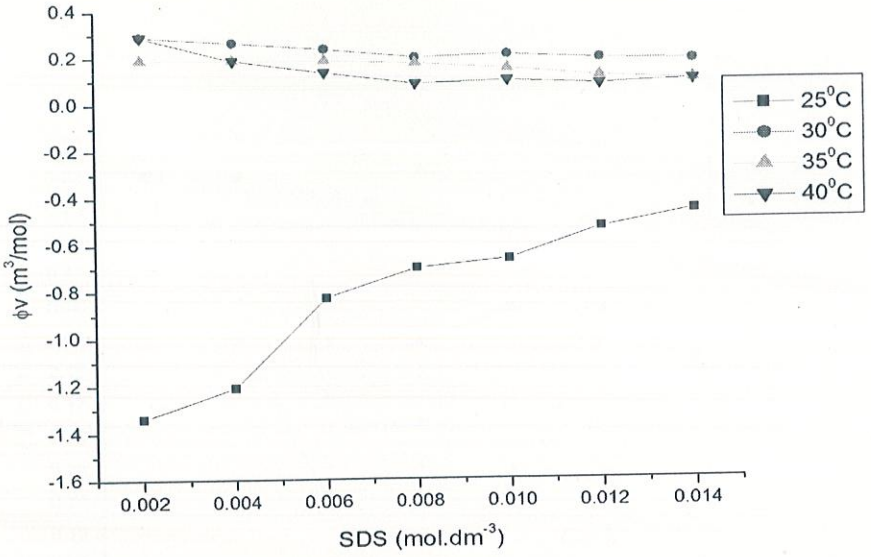

Figure 10(a). Apparent molar volume (Φ_v) as a function of SDS in 0.001mol.dm^{-3} BHA at different temperatures.

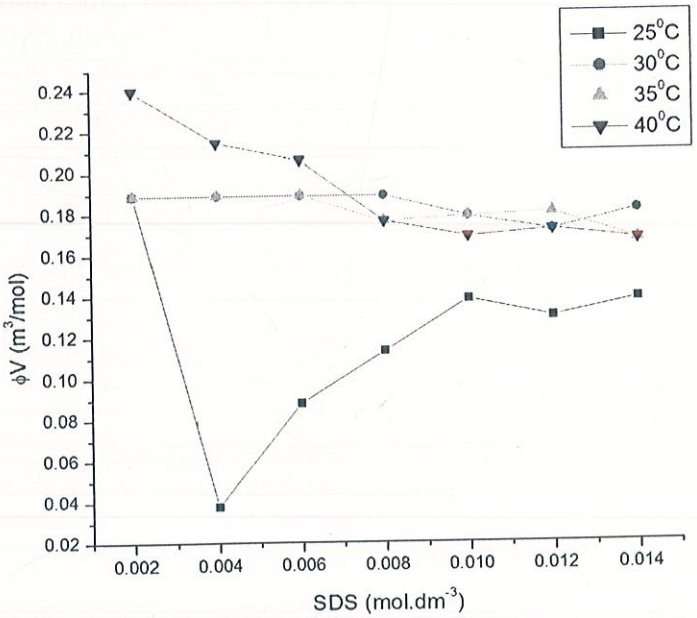

Figure 10(b). Apparent molar volume (Φ_v) as a function of SDS in 0.002mol.dm^{-3} BHA at different temperatures.

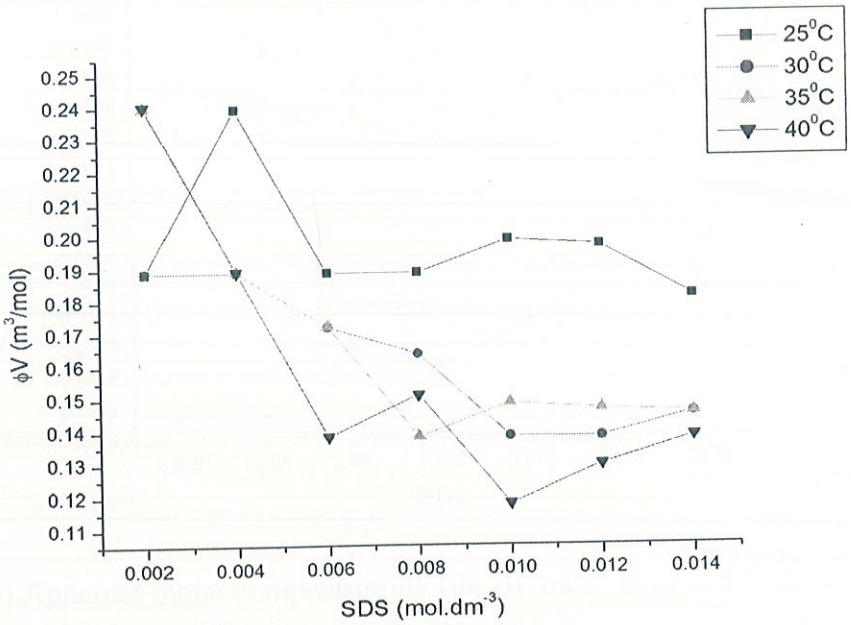

Figure 10(c). Apparent molar volume (Φ_v) as a function of SDS in 0.003 mol.dm^{-3} BHA at different temperatures.

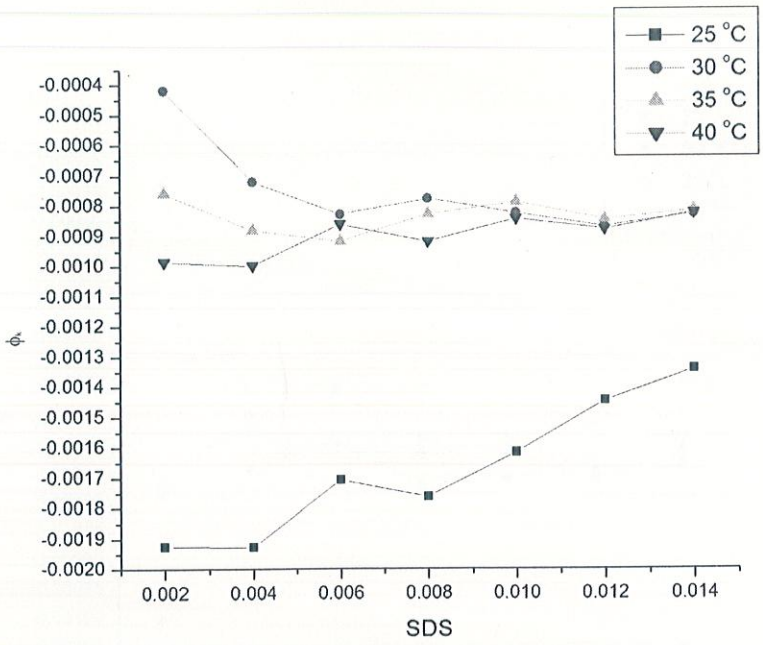

Figure 11(a). Apparent molar compressibility (Φ_k, m^3 mol^{-1} atm) as a function of SDS in 0.001 $mol.dm^{-3}$ BHA at different temperatures.

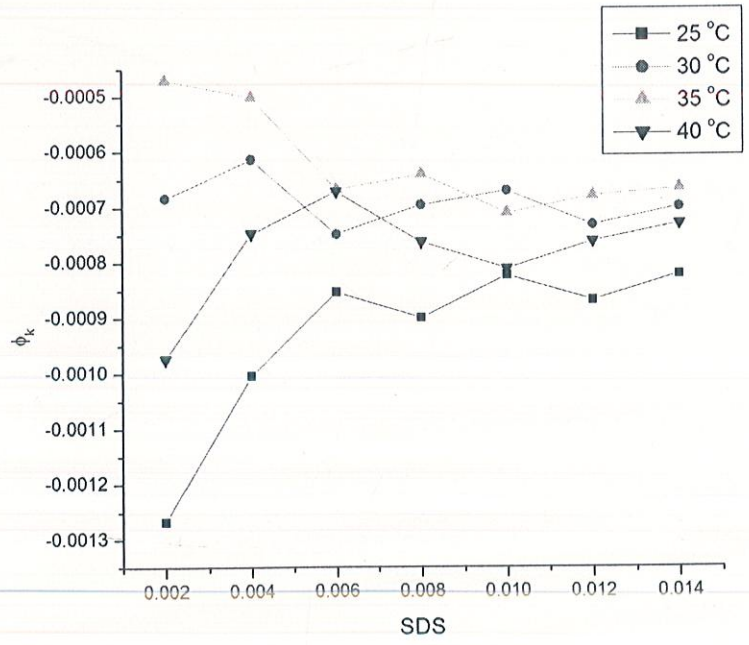

Figure 11(b). Apparent molar compressibility (Φ_k, m^3 mol^{-1} atm) as a function of SDS in 0.002 $mol.dm^{-3}$ BHA at different temperatures.

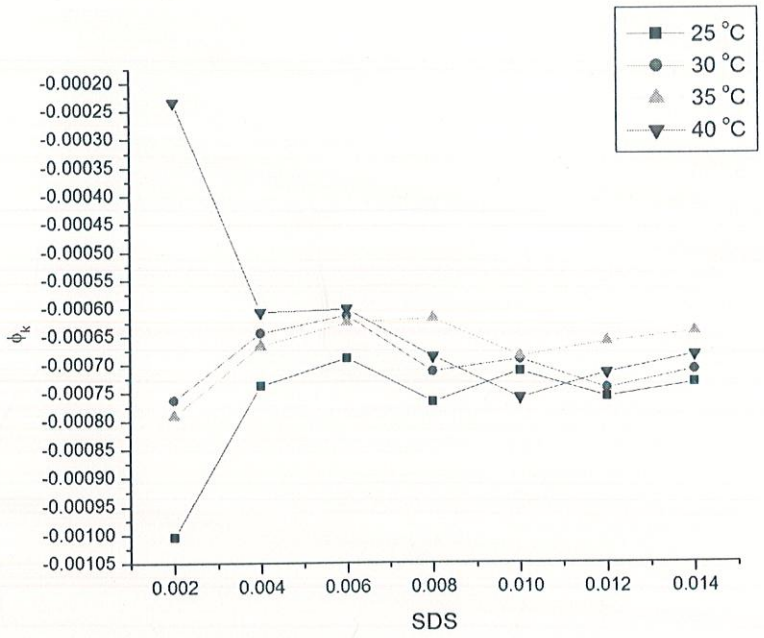

Figure 11(c). Apparent molar compressibility (Φ_k, m^3 mol^{-1} atm) as a function of SDS in 0.003mol.dm^{-3} BHA at different temperatures.

CONCLUSIONS

5. Conclusions

Experimental data at different temperatures (25-40°C at intervals of 5°C) of conductivity, density, viscosity and ultrasonic velocity of BHA and SDS in pure aqueous solution have been reported in this dissertation. The thermodynamic parameters were calculated using CMC from electrical conductivity measurements. A significant change in $\Delta H°_m$, $\Delta G°_m$ and $\Delta S°_m$ was observed with increase in concentration of BHA and temperature. $|T\Delta S°_m|$was found to be larger than $|\Delta H°_m|$ indicating micelle formation is entropy driven whereas $\Delta H°_m$ and $\Delta G°_m$ value suggested feasibility of system which is exothermic in nature. Likely, viscometric study was also found to be temperature dependent and positive viscosity B-cofficients are indicative of strong solute-solvent interactions. However,from the graphs of Φ_v structural changes as well as interactions were observed up to 8 $mM.dm^{-3}$ concentrations whereas from 8-14 $mM.dm^{-3}$a consistency was observed with slight changes. This observation supports the conductivity data where micelle formation is much easier than nearby $8mM.dm^{-3}$.

APPENDIX

APPENDIX - I

Density d (g/ml), coefficient of viscosity η(centipoise) and velocity of sound v (ms^{-1}), of SDS in aqueous solution of 0.001 $mol.dm^{3}$, 0.002 $mol.dm^{-3}$ and 0.003 $mol.dm^{-3}$ BHA at 25°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	d	η	v	d	η	v	d	η	v
0.002	0.9920	0.6858	1249	0.9976	0.7753	1269	0.9948	0.8835	1289
0.004	0.9947	0.7097	1251	0.9984	0.7999	1270	0.9948	0.9123	1290
0.006	0.9954	0.7335	1253	0.9986	0.8242	1271	0.9952	0.9367	1291
0.008	0.9966	0.7574	1256	0.9988	0.8485	1273	0.9954	0.9778	1293
0.010	0.9982	0.7814	1257	0.9989	0.8799	1274	0.9955	1.0307	1294
0.012	0.9985	0.8175	1258	0.9993	0.9406	1276	0.9957	1.0909	1296
0.014	0.9991	0.8536	1259	0.9995	0.9890	1277	0.9961	1.1708	1297

Density d (g/ml), coefficient of viscosity η (centipoise) and velocity of sound v (ms^{-1}), of SDS in aqueous solution of 0.001 $mol.dm^{-3}$, 0.002 $mol.dm^{-3}$ and 0.003 $mol.dm^{-3}$ BHA at 30°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	d	η	v	d	η	v	d	η	v
0.002	0.9933	0.7709	1269	0.9962	0.7609	1279	0.9934	0.7882	1298
0.004	0.9934	0.7857	1271	0.9964	0.7808	1280	0.9936	0.8618	1299
0.006	0.9936	0.8079	1273	0.9966	0.8104	1282	0.9939	0.9429	1300
0.008	0.994	0.845	1274	0.9968	0.8719	1283	0.9942	1.0338	1302
0.01	0.9941	0.8818	1276	0.9971	0.9336	1284	0.9947	1.1569	1303
0.012	0.9945	0.9312	1278	0.9974	1.0322	1286	0.995	1.2651	1305
0.014	0.9948	0.9805	1279	0.9975	1.1184	1287	0.9952	1.3733	1306

Density d (g/ml), coefficient of viscosity η (centipoise) and velocity of sound v (ms^{-1}), of SDS in aqueous solution of 0.001 $mol.dm^{-3}$, 0.002 $mol.dm^{-3}$ and 0.003 $mol.dm^{-3}$ BHA at 35°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	d	η	v	d	η	v	d	η	v
0.002	0.9941	0.6858	1290	0.9947	0.7336	1289	0.9918	0.7386	1309
0.004	0.9943	0.7097	1292	0.9949	0.7693	1290	0.9921	0.786	1310
0.006	0.9945	0.7335	1294	0.9951	0.8073	1292	0.9924	0.8335	1311
0.008	0.9948	0.7574	1295	0.9954	0.8762	1293	0.9929	0.8882	1312
0.01	0.9953	0.7814	1296	0.9956	0.9356	1295	0.9931	0.9404	1314
0.012	0.996	0.8175	1298	0.9958	0.9832	1296	0.9934	1.0116	1315
0.014	0.9966	0.8536	1299	0.9962	1.031	1297	0.9937	1.0709	1316

Density d (g/ml), coefficient of viscosity η(centipoise) and velocity of sound v (ms^{-1}), of SDS in aqueous solution of 0.001 $mol.dm^{-3}$, 0.002 $mol.dm^{-3}$ and 0.003 $mol.dm^{-3}$ BHA at 40°C.

	0.001			0.002			0.003		
[SDS] Mol dm^{-3}	d	η	v	d	η	v	d	η	v
0.002	0.9947	0.6655	1312	0.9927	0.6147	1300	0.9899	0.6399	1318
0.004	0.9951	0.6861	1314	0.9929	0.6328	1301	0.9902	0.6513	1320
0.006	0.9956	0.7203	1315	0.9931	0.6622	1302	0.9907	0.6853	1321
0.008	0.9963	0.7683	1317	0.9935	0.7165	1304	0.9909	0.7192	1323
0.01	0.9966	0.8137	1318	0.9938	0.7709	1306	0.9915	0.7758	1325
0.012	0.9972	0.8707	1320	0.994	0.8341	1307	0.9917	0.8367	1326
0.014	0.9974	0.9162	1321	0.9943	0.8975	1308	0.9919	0.9246	1327

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