Thermodynamics and Acoustical Studies of Rutin trihydrate in the Presence of Non-ionic Surfactant Triton X-100 in a Hydro-Ethanolic Mixtures

A MAJOR PROJECT REPORT

Submitted in partial fulfillment of the requirements for the award of the

degree of

BACHELOR OF TECHNOLOGY

IN

BIOTECHNOLOGY

Under the

supervision of

Dr. Poonam Sharma

(ASSOCIATE PROFESSOR)

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May, 2025

DECLARATION

We hereby declare that the work represented in the project report entitled **"Thermodynamics and Acoustical Studies of Rutin trihydrate in the Presence of Non-ionic Surfactant Triton X-100 in a Hydro-Ethanolic Mixtures"** submitted towards partial fulfillment of the requirements for the award of the degree in Bachelor of Technology in Biotechnology at the Jaypee University of Information Technology, Waknaghat is an original work carried out under the supervision of Dr. Poonam Sharma. The work has not been submitted elsewhere for the reward of any degree/diploma. We are fully responsible for the contents of the major project report.

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CERTIFICATE

This is to certify that the work which is being presented in the project report **"Thermodynamics and Acoustical Studies of Rutin trihydrate in the Presence of Non-ionic Surfactant Triton X-100 in a Hydro-Ethanolic Mixtures"** in partial fulfillment of the requirements for the award of the degree of Bachelor of Technology in Biotechnology submitted to the Department of Biotechnology and Bioinformatics, Jaypee University of Information Technology, Waknaghat is an authentic record of work carried out by Mr. Sangay Wangchuk and Mr. Tshering Dendup during a period from August, 2024 to May, 2025 under the supervision of Dr. Poonam Sharma (Associate Professor), Department of Biotechnology and Bioinformatics, Jaypee University of Information Technology.

The above statement is correct to the best of our knowledge.

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Abstract

The thermodynamic and the acoustical studies were conducted to study the interactions between flavonoids rutin trihydrate, and the non-ionic surfactant triton X-100. Rutin trihydrate, a significant flavonoid, is known for its antioxidant and antimicrobial properties. These experiments sought to learn about molecular interaction and how different conditions alter these interactions. Five ethanol concentrations were used in the experiments: 0%v/v, 10%v/v, 30%v/v, 50%v/v, and 80%v/v. These were tested at a variety of temperatures of 20℃, 25℃, 30℃, 35℃, and 40℃. Additionally, the different concentrations of rutin trihydrate of 1mM, 2mM, and 3mM were used. Several parameters were measured during the studies, including density, surface tension, and ultrasonic velocity. These measurements were crucial for calculating various thermodynamic and acoustical studies including apparent molar volume, apparent molar compressibility, and changes in enthalpy, change in entropy, and change Gibbs energy of micellization. The results of these studies are important for examining the interactions within the system. Understanding these interactions can help in determining the optimal concentrations of rutin trihydrate and triton X-100 for preparing topical formulations.

Keywords: Rutin trihydrate; Critical Micelle Concentration; Thermodynamic; Change in Enthalpy; Change in Gibbs Energy.

CHAPTER 1

1. Introduction

The thermodynamics plays an important role in biophysics and chemical science. It acts as an essentials tool in identifying the character of reactions that take place in systems as well as to comprehend the process of conversion of heat in chemistry, engineering, biotechnology, pharmacy and biophysics [1]. Physical and chemical properties of active molecules are vital for drug delivery as well as for subsequent investigations. Some physicochemical parameters are surface tension, density and ultrasonic velocity, which are of considerable relevance in formulation studies. At the same time, study of the acoustics parameters such as the apparent molar volume and the molar compressibility too gives valuable data on molecular interactions in investigations. Using the interactions in a system it is possible to evaluate active and concentrated drugs for development studies [2].

Among the secondary metabolites, flavonoids are the most recognized for their therapeutic properties in the pharmaceutical market. They are rich specifically in a buckwheat, citrus fruits and apples, and berries [3]. They have been the subjects of considerable investigation because they possess significant antioxidant, anti-inflammatory and healing effects. According to biopharmaceutical classification, rutin trihydrate is a BCS class II compound, which remains low solubility and high permeability. Thus, its biological properties can be restricted because of solubility issues. This compound has little water-solubility which restricts its uptake, yet has high permeability which makes it move through biological membranes effectively [4]. In general, it is stated that the elimination half-life of rutin is few hours' clears suggesting that this compound is eliminated at rapid rates in the body. Rutin exhibits low biopharmaceutical properties which means that solubility and permeability properties are low; in other words, little of the drug is actually taken into the body. Several strategies are under investigation to improve their aqueous solubility and pharmacokinetic profile of the compounds including nanoparticle surface coating, incorporation into ethosomes or other new drug delivery systems [5]. This process may help to prevent rather active destruction of rutin and let it work longer that can have therapeutic effects.

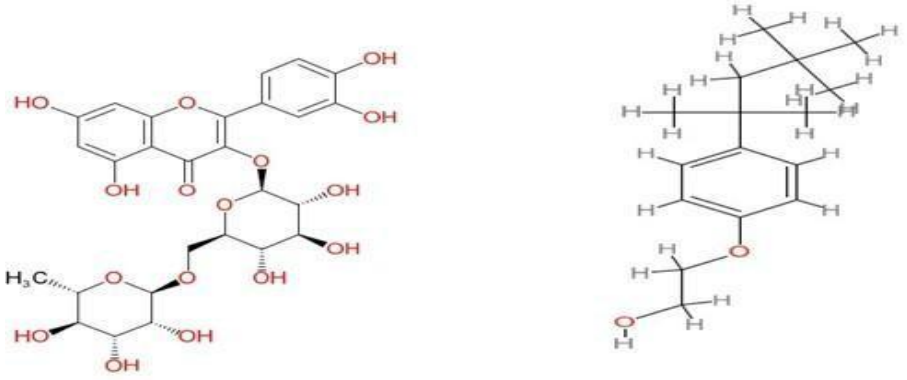


Fig. 1: Chemical structure of rutin trihydrate and triton X-100

The phospholipids that are natural surfactants are able to absorb on interfacial membranes and increase the permeability of the membranes. Certain of these amphiphilic surfactants can effectively lower the interfacial tension of two thick phases including water and oil. Surfactants are chemicals that act as agents that either lowers the tension between a liquid and a solid or between two liquids. Surfactants are largely divided into categories of non-ionic, cationic or anionic depending on the type of charge the component possesses. Triton X-100 is non-ionic surfactant. This surfactant, at their CMCs, is documented to form micelle aggregates which are a cluster of micelles. This characteristic of surfactants makes them to have the ability to dissolve, disperse, suspend and transport substances [6].

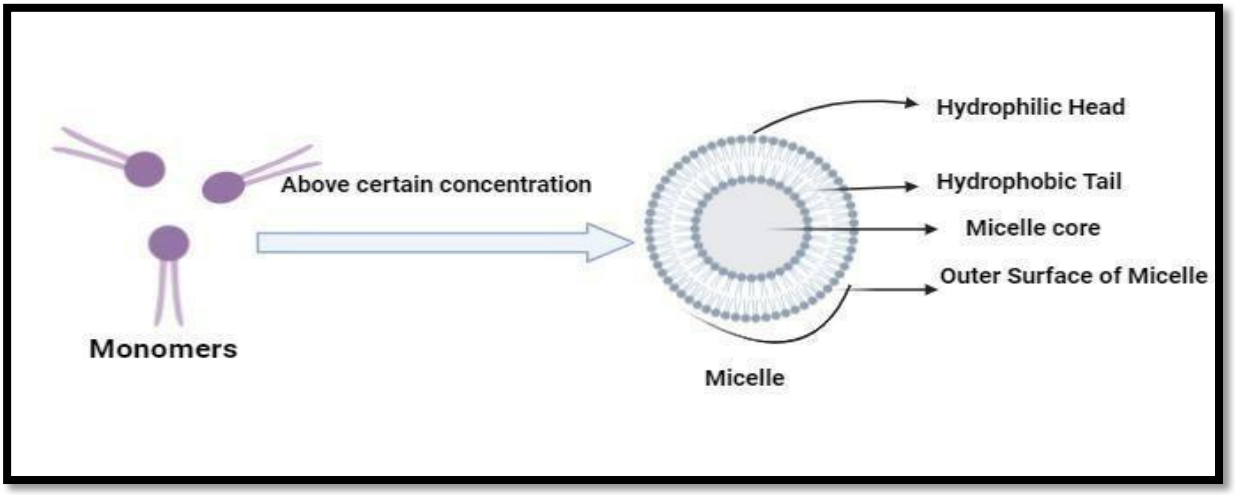


Fig.2: Micellization process

The primary purpose of surfactants is to decrease the surface tension of solution and for the solubility of the molecules. The physiochemical properties, including surface tension determination, play a vital role in discovering molecular interaction between rutin and triton X-100. The surface tension is found to reduce with increase in the concentration of the surfactant in the system. These investigations give detailed understanding of the behavior of Rutin in surfactant solution that determine its stability and solubility and the possibility of its uses in areas like the drug delivery system among others [7]. Based on nature of charge carried at their hydrophilic head groups, surfactants are predominantly categorized as follows [8]:

(a) Anionic surfactants: The hydrophilic ends of these surfactants are negatively charged. Because of their low production costs and linear chain topologies, such as sodium dodecyl sulfate (SDS), they are frequently used in the formulation of medicinal and cosmetic products.

(b) Cationic surfactants: These surfactants are composed of quaternary ammonium compounds, which give them hydrophilic ends with a positive charge. Their ability to absorb at negatively charged surfaces makes them stable compounds that are widely utilized in topical products, such as cetyltrimethyl ammonium bromide (CTAB).

(c) Non-ionic surfactants: These surfactants have hydrophilic ends that are charge-free. Because they dissolve in both aqueous and non-aqueous solvents, such as triton X-100 and polysorbates (Tween 20, Tween 80), they are useful in the medical industry.

Critical Micelle Concentration (CMC) is the quantity of surfactants that in solution brings about the presence of micelles. Micelles are also spherical structures made of the hydrophobic chains of the surfactants pointing toward the center of the micelle with the polar heads pointing toward the outer side facing the water. Poorly permeable drug molecules and poorly water-soluble molecules can get entrapped within the micellar structure so that they can permeate easily across the cell membrane and exert their desired action at the site. The type of adhesive and cohesive forces the amphiphilic character of surfactants creates between the micelles and drugs controls the type of interaction taking place within the system [9]. Such a property of micelle formation is extremely useful in drug delivery application especially when the product to be delivered is a poorly water soluble compound like some flavonoids since it increases the solubility and increases the bioavailability rate [10].

In order to identify stable and efficient concentrations of rutin and surfactant that may be used in formulation development experiments, the interaction investigations of rutin trihydrate and triton X-100 have been described in this study. The type of interactions and reactions taking place in the system has been determined by a number of physico-chemical investigations, including those involving surface tension, density, and ultrasonic velocity.

A number of thermodynamic parameters have been computed using the micellization behavior of the surfactant-flavonoids system, including standard enthalpy change, standard entropy change, and standard Gibbs free energy change [11]. The acoustic parameters, apparent molar volume, and apparent molar compressibility have all been determined using ultrasonic velocity measurements. The experiments have been conducted in five different hydro-ethanolic concentrations i.e. 0% v/v, 10% v/v, 30% v/v, 50% v/v, and 80% v/v to study a stable solvent system at various temperatures of 20℃, 25℃, 30℃, 35℃, and 40℃.

Examining how a drug interacts with bio membrane is crucial in the early phases of drug development. Depending on the type of additives and solvent vehicles being dissolved, these interactions can be ionic, covalent, hydrophobic, hydrophilic, electrostatic, or dipole-dipole.

There are fewer failures in the drug discovery and development process when such interactions are known early on [12]. Furthermore, knowing the thermodynamic characteristics helps determine whether or not the system can undergo reactions and is thermodynamically stable. Consequently, studies and interactions within the system for medication formulation have established the acoustical and thermodynamic characteristics [13].

CHAPTER 2

2. Literature survey

Jiangxiu Niu et al. (2022) have studied the Pentapeptide modified ethosomes for enhanced skin retention and topical efficacy activity of indomethacin. Problems associated with topical anti inflammatory include poor penetration and retention of the drug where it is needed. Therefore, improving these challenges will help reduce side effects caused by the absorption of drugs into body organs and improve the treatment of topical medications. Pentapeptide (KTTKS) is a signal peptide found in skin tissue that can be recognized and bound by the recognition signal. In this study, we synthesized novel indomethacin (IMC)-loaded KTTKS-modified ethosomes (IMC-KTTKS-Es) and examined their physical and chemical properties and local activity. The results showed that the prepared IMC-KTTKS-Es had a particle size of about 244 nm, the IMC encapsulation efficiency (EE) was more than 80%, and support release was found. In vitro percutaneous permeation studies showed strong skin retention after drug loading into IMC-KTTKS-E. Confocal laser scanning microscopy also showed skin improvement with IMC-KTTKS-E. Additionally, IMC-KTTKS-Es have been shown to improve local analgesic and anti-inflammatory activity without damaging the skin. This study shows that IMC-KTTKS-Es may be an effective drug with good safety in the treatment of skin diseases [14].

Subheet Jain et al. (2016) Formulated and Evaluated the Ethosomes for Transdermal Delivery of Lamivudine. The aim of this study is to use visualization techniques and cell studies to investigate the intercellular and intracellular drug delivery mechanisms of ethanol. Ethanosome formulations were prepared using lamivudine as a model drug and characterized in vitro, ex vivo and in vivo. Transmission electron microscopy, scanning electron microscopy, and fluorescence microscopy were used to determine the effect of ethosomes on skin structure. The cytotoxicity and cellular uptake of ethosomes in the body were determined using a T lymphocyte cell line (MT-2). Optimization of the ethosomes showed 25-fold greater transdermal flux through rat skin (68.4 ± 3.5 g/cm2/h) compared to liquid lamivudine (2.8 ± 0.2 g/cm2/h). The results of the cellular uptake study showed that the intracellular uptake of Ethosomes was higher (85.7% ± 4.5%) than in solution (24.9% ± 1.9%). Results from behavioral studies indicate that lipid degradation as well as the flexibility of vesicles is important in skin development [15].

V. Abbot et al. (2021) have studied interaction between SDS and Rutin through thermodynamic, acoustic, and 1H NMR studies. The values for CMC were carried out to demonstrate spontaneous and exothermic interactions between the molecules. Strong intermolecular interactions were confirmed through 1H NMR analysis to be crucial for pharmaceutical formulations [2].

Naheed Akhtar et al. (2024) have developed and evaluated Tocopherol succinate loaded Ethosomes. Tocopherol is known as an antioxidant and moisturizer. Tocopherol succinate (TS) is widely used in many skin products, especially anti-aging and skin whitening formulations. Here, we developed and added the TSEG feature to increase skin permeability while increasing the stability of the designed formulations. The size of the formed Ethosomes vesicles is 250 nm, allowing TS to penetrate the stratum corneum. Measurements are based on color, odor and phase separation. Transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR), X-ray diffraction spectroscopy (XRD), zeta potential (ZP), and particle size (PS) were used for TSEG physical characterization. In vitro dissolution and ex vivo permeation studies (using a Franz diffusion cell) were performed for both TSEG and CEG formulations. Human women (N = 34) were used to evaluate in vivo biophysical parameters, including erythema, melanin, moisture content, sebum level, and skin elasticity. The developed formulations are thermally stable for 3 months. TSEG6 formulation showed the highest EE with 99.89 ± 1.32% whereas TSEG1 displayed the lowest EE with 93.88 ± 1.32%. The TSEG formulation developed by has been shown to be effective, safe (no side effects), stable (at least 3 months), and easy to use topically, improving skin care and skin integrity [16].

Harjas Saini et al. (2022) investigate the physico-chemical properties of a vancomycin hydrochloride solution-via viscosity, specific gravity, and thermodynamic parameters-the investigations were carried out. The critical micelle concentration (CMC) was determined, indicating favorable micelle formation. Analyses of electrostatic forces prevail over the lower concentrations whilehydrophobic forces dominate the higher concentrations [3]. *Jiesi Xie et al (2018)* have prepared the nanocarriers by encapsulating Rhodamine B (RB) as a model drug and created hyaluronic acid-containing ethosomes (HA-ES) as a transdermal drug delivery approach. As per the results, the HA-ES-RB is spherical, has good separation, good stability, and particle size under 100 nm. It was found that HA-ES-RB showed better permeability than ES-RB. This research develops ethosomes containing hyaluronic acid that is able to deliver drugs quickly, efficiently and safely across the skin barrier [17].

Rohan Raj Patekar et al. (2022) developed and evaluated Ethosomal Gel and Non-ethosomal Gel of sesbania grandiflora leaf, which can deliver drugs to the site more efficiently than commercially available gel formulations and overcome problems associated with oral administration of the drug. Transdermal drug delivery is a tool used to overcome changes in pH, food intake, and the digestive tract that may affect the oral absorption of the drug. Compared to liposomes or hydroalcoholic solutions, ethosome systems can deliver fluorescent probes to the skin at a greater and deeper level. The treatment was prepared and measured with ethanol, lecithin, propylene glycol, and glycerol. Lecithin (phospholipid) is used as the vesicle-forming component, and polyethylene glycol and ethanol are used as skin penetrating agents. Ethosomal gel provides 4-5 times more drug release than non-ethosomal gel. Ethosomal gel solved the problems related to the transport of drugs in water, peptides, potent drugs and the release of various drugs [18].

Lijun Zhang et al. (2020) developed and evaluated a new multi Ethosomes for dermal delivery of terbinafine hydrochloride (TH) as a new method for the treatment of fungal infections. TH-loaded ME was successfully prepared using cinnamaldehyde as a penetrating agent. The average diameter of ME is approximately 100 nm and has a uniform size distribution. The drug encapsulation rate or penetration rate is as high as 86% ± 1.4%. MEs exhibit outstanding colloidal stability and no drug leakage after 2 months of storage. Attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) demonstrated that increased mobility of the stratum corneum by ME improved target performance compared to commercial LamisilÂ® cream. It has also been shown that skin irritation and allergies do not irritate the skin. It has been shown in vitro to have enhanced antimicrobial activity against Candida albicans as measured by minimum inhibitory concentration (MIC) assay. This study expands the formulation of ME for the treatment of fungal infections of the skin [19]

Shish Goindi et al. (2014) developed Ethosomes-based topical delivery system of antihistaminic drug for treatment of skin allergies. Cetirizine is indicated for the treatment of allergic reactions such as insect bites, atopic and contact dermatitis, eczema and urticaria. This study involved the development of a novel ethanol-based topical formulation of cetirizine dihydrochloride for effective delivery. The ex vivo permeation studies through mouse skin showed that cetirizine-loaded ethosomal vesicles had the highest permeability rate of (16,300 ± 44/200 mg/h/cm2) and retention rate of (20.686 ± 0.517 mg/cm2).

In vivo pharmacodynamic evaluation of optimized formulations was assessed against oxazolone-induced atopic dermatitis (AD) in mice. The results indicate that ethosomes are effective carriers for the delivery of the antihistamine cetirizine for the treatment of atopic dermatitis [20].

Yubaraj Ghimire et al (2020), the thermodynamic studies and contact angles of SDS and CTAB in acetone-water mixtures at several temperatures were determined. Primary characteristics such as CMC and ΔG°m were measured through conductivity. The measurements showed that the CMC increased with temperature and acetone altered the micellization and thermodynamic properties. Contact angles rose with decreasing concentrations of CTAB and SDS in the mixtures [4]. *V. Abbot et al. (2021)* the physiochemical investigations of Rutin and CTAB in hydro-ethanolic solvent systems were carried out in terms of thermodynamic, acoustic, and spectroscopic studies. The measurements of CMC values, correspondingcalculations of thermodynamic and acoustical parameters were carried out. The results indicate that the reactions are exothermic, and the micellization process could be influenced by hydrophobic interactions [1].

Kampanart Huanbutta et al (2022) have generated and evaluated Zingiber zerumbet Linn Rhizome Ethosomes Loaded Deep Layer Skin for Fungal Skin Infection. The aim of this work is to produce an ethosomes which would include Zingiber zerumbet (L.) Smith. With the cold method, they only manufactured ethosomes through the use of40% (v/v) ethanol and 1% (w/v) phosphatidylcholine in the synthesis formula. The vesicle form of the ethosomes can be recognized using TEM, showing diameters to be in between 205. 6 to 368. 5 nm. The encapsulation efficiency of ethosomes is 31. 58% and this will inhibit the growth of Candida albicans at a concentration of 312. 5µg/mL. This research provides the evidence of loading Z. zerumbet (L.) rhizome extract into ethosomes. Other clinical applications of the study can be made through the ex vivo and in vivo penetration [21].

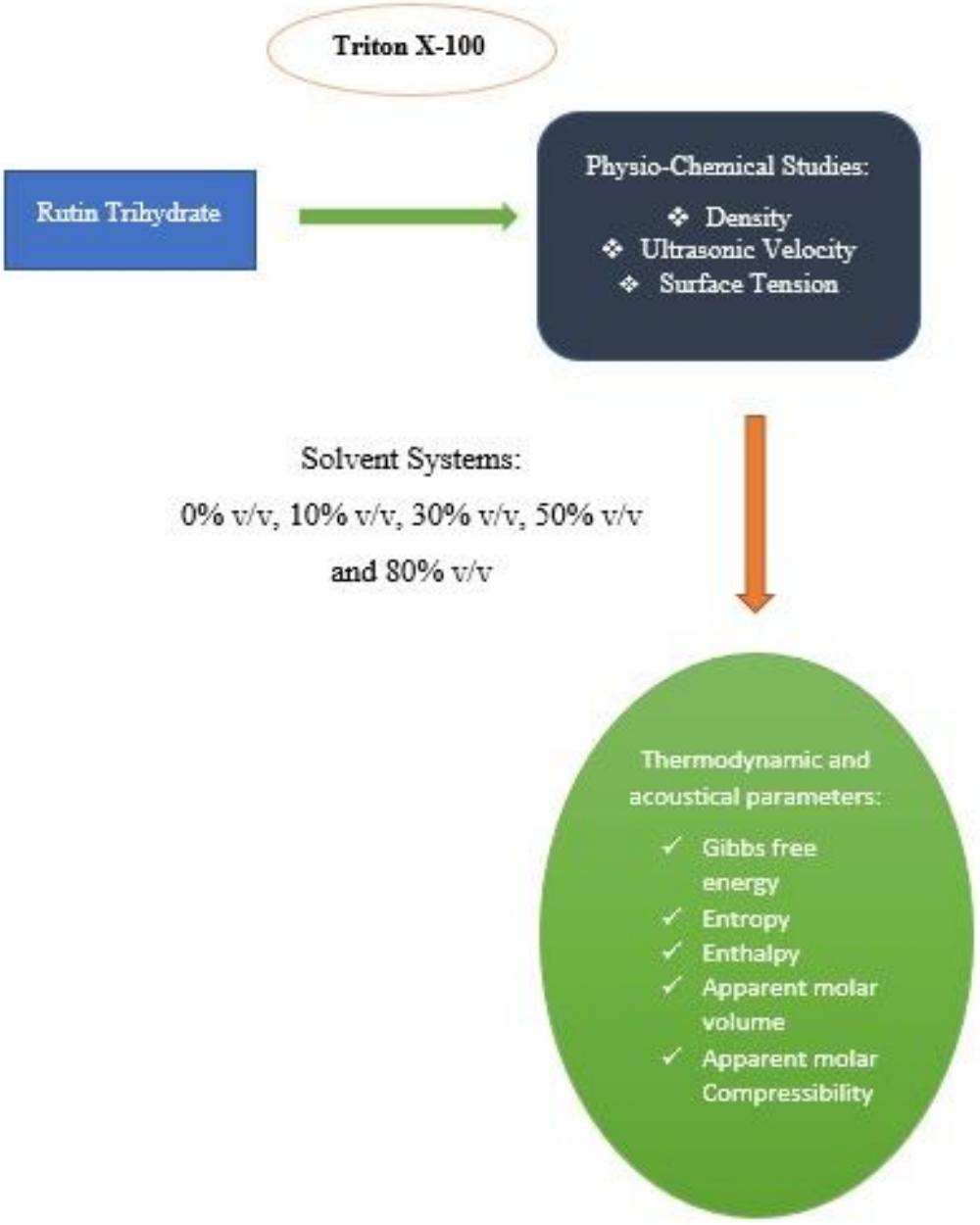
SiddhodhanS et al. (2013) studied on Ethosomes as mode for transdermal delivery of an anti diabetic drug. They have prepared and evaluated Ethosomes as transdermal delivery for repaglinide (RPG). Materials and methods: RPG-loaded Ethosomes were prepared by cold method using dipalmitoyl phosphatidyl choline and ethanol as raw materials. The Fourier transforms infrared spectroscopy and differential scanning calorimetry is used for characterization.

These were evaluated for vesicle size, encapsulation efficiency, and ex vivo skin permeability. Gel containing optimzsed Ethosomes was studied for ant diabetic activity in rats. RPG Ethosomes size of 0.171-1.727 micrometer and the entrapment rate of 75-92% were obtained. They showed a higher permeability through rat skin compared to the free drug and its hydro alcoholic drug (64–97% of the dose). In vivo, RPG ethosomes induces anti diabetic effect [22].

Nimisha et al. (2017) Formulated and Evaluated Performance of Berberis Aristata Extract Loaded Ethosomal Gel. The aim of this research project is to prepare ethosome of Berberis aristata extract Ethosomes and to evaluate vesicle shape, size, polydispersity index (PDI), zeta potential (ZP), and encapsulation efficiency (EE). Soybean phosphatidylcholine (1-3%) and ethanol (10-40%) were prepared and produced by cold method. The size of Ethosomes ranged from 110.98-357.34 nm, PDI from 0.114 to 1.56, and zeta potential from -20.0 to -39.4 mV. Morphological studies showed that the monolayer structure showed a smooth surface in transmission electron microscopy and phase contrast microscopy. The entrapment efficiency of Ethosomes varies from 48.05% and 92.08% [23].

CHAPTER 3

3. Overview of the study



CHAPTER 4

4.1. Rationale of the study

- ✓ Physicochemical studies will facilitate the determination of the optimal concentration of drugs and surfactants for transdermal formulations.
- ✓ The thermodynamic and acoustic analysis shows how stable the drug molecules are, how they interact with triton X-100, and how they aggregate together.
- ✓ Although rutin, a natural flavonoid, exhibits notable pharmacological properties, its low solubility and permeability limit its clinical application.
- ✓ Ethosomes are alcoholic preparation which has high penetration capability as compared to other vesicular systems like liposome etc.
- ✓ The ethosomal formulation of rutin enhances its bioavailability and permeability.
- ✓ The non-ionic surfactant triton X-100 proves beneficial for these studies because it can form micelles, aiding in solubilization and influencing the interaction of these compounds in solutions.

4.2. Objectives of the study

- ✓ To investigate the density and surface tension to obtained the Critical Micelles Concentration (CMC).

- ✓ To determine thermodynamics parameters like changes in enthalpy, change in entropy, and Gibbs energy using the CMC.

- ✓ To investigate ultrasonic velocity and density to determine acoustical parameters like apparent molar volume and apparent molar compressibility.

CHAPTER 5

5. Materials and Methodology

5.1. Chemicals

The surfactant, triton X-100 and the flavonoid, rutin trihydrate which is 97% pure was purchased from Sigma-Aldrich and it was used without any purification. The ethanol was purchased from Merck KGaA, Darmstadt, Germany. The chemical structure of rutin and triton X-100 was given in the *figure 1*. The distilled water was prepared newly using the Millipore Elix Distillation Assembly having the pH values within the range of 6.5– 7.0.

5.2. Methodology and equipments used

The main solution consists of rutin where its concentration ranging from 1mM, 2mM and 3mM, were prepared in different hydro-ethanolic concentrations. The stock solutions were prepared using surfactant triton X-100 of five different hydro-ethanolic concentrations (0% v/v, 10% v/v, 30% v/v, 50% v/v, 80% v/v) at temperatures ranging from 20℃, 25℃, 30℃, 35℃, and 40℃. Triton X-100 concentrations ranging from 0-0.4mM were generated from stock solutions. These concentrations were used for calculation of density, surface tension, and ultrasonic velocity.

5.2.1. *Density Calculation*

For the calculation of the density, the bottle of specific gravity and weighing machine were used. Densities were calculated for the ethanol concentrations for all the rutin concentrations and at different range of temperature mentioned above. The empty specific gravity bottle weight were noted and assigned the notation W_1. The weight of specific gravity bottle filled with distilled water were noted and assigned the notation W_2. The weight of specific gravity bottle filled solutions were noted and assigned the notation W_3.

The subsequent formula was used for calculating the density;

$$\rho = (W_3 - W_1) / (W_2 - W_1) \times \rho W$$

Where, ρW is the density of the water at the specific temperature, W_3 is weight of specific gravity bottlefilled with solutions, W_2 is weight of the specific gravity bottle with water and W_1 is weight of the empty specific gravity bottle.

The densities of the water at the specific temperature are given as follows;

- 20°C - 0.998 g/cm^3
- 25°C - 0.997 g/cm^3
- 30°C - 0.995 g/cm^3
- 35°C - 0.994 g/cm^3
- 40°C - 0.992 g/cm^3

Fig. 3: Density measurement using specific gravity bottle and weighing machine

5.2.2. Determination of Surface Tension

Biolin Scientific Theta Lite Tensiometer was used to determine the surface tension. For this, the pendant drop method was employed as represented in *figure 4*. Densities were calculated to determine the surface tension and then using density values, surface tensions were calculated. These surface tensions were used for the determination of CMC values where it helps in determining the thermodynamic parameters which are useful for formulations and novel drug delivery systems [24].

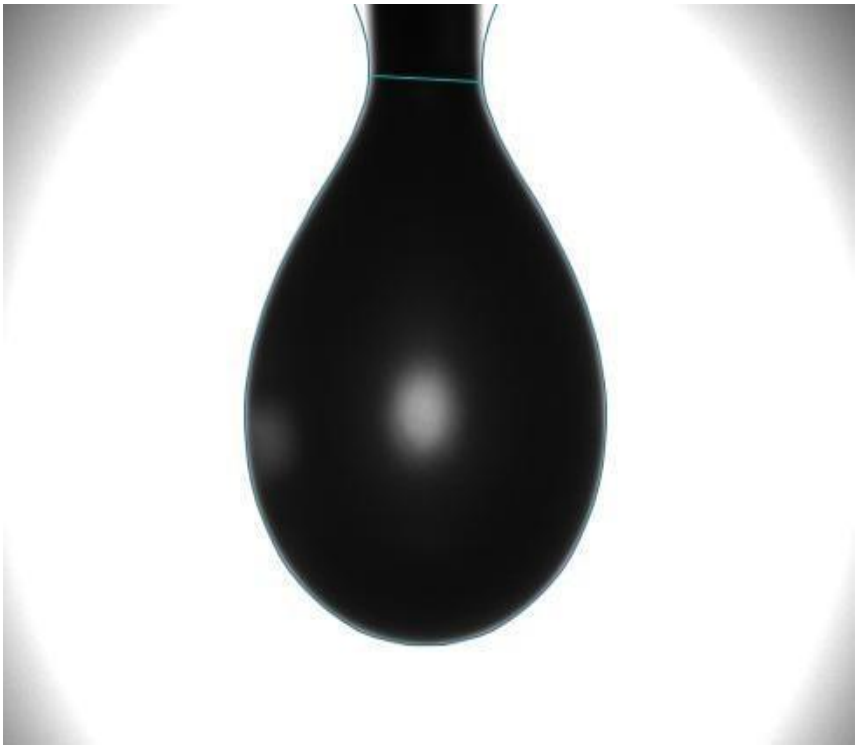


Fig.4: Surface tension measurement by pendant drop

5.2.3. Determination of CMC values

The Critical Micelles Concentration (CMC) was calculated from the surface tension values. CMC were calculated by plotting the graphs between the surfaces tension values and concentration of triton X-100. From the graph, pre-micelle and post-micelle were determined and tangent line was drawn from this point. The two connection/intersection points were considered as CMC values [25]. For general method of CMC measurement by plotting the graph of surface tension, it is shown in the *Fig 5*.

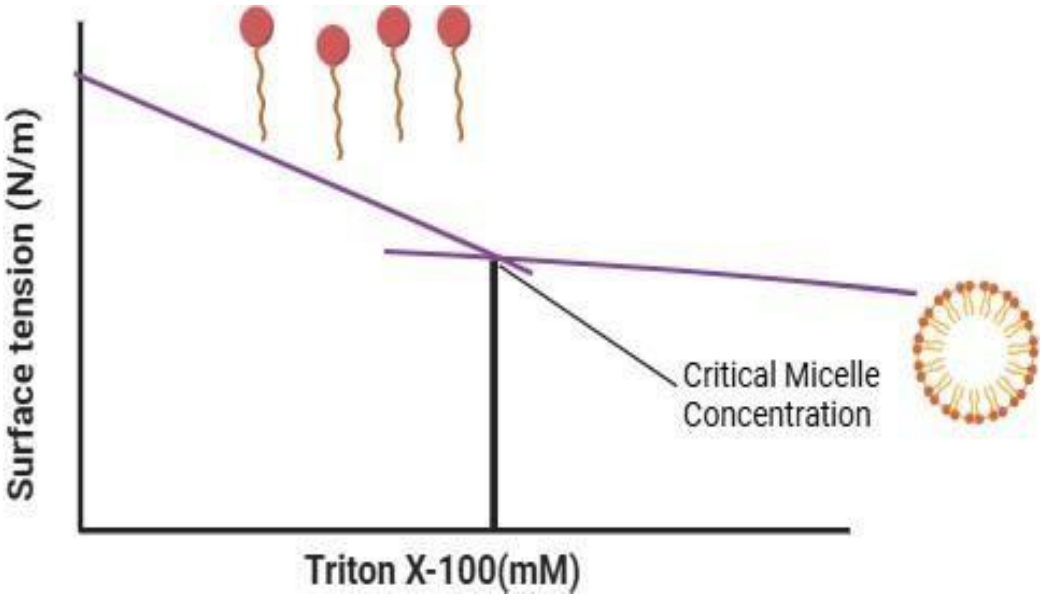


Fig. 5: Graphical representation of CMC determination

5.2.4. Determination of thermodynamics parameters

The CMC data were further converted into mole fraction i.e. X_{cmc} used for the calculation of various thermodynamics parameters such enthalpy ($\Delta H^o m$), entropy ($\Delta S^o m$) and Gibb's free energy ($\Delta G^o m$) of the micellization. The following formulae were used to calculate the thermodynamics parameters;

$$\Delta H°\text{m} = -RT^2 \left[\text{d}\left(ln X_{CMC}\right)/T\right] \quad \text{.....(1)}$$

$$\Delta G°\text{m} = -RT\left(ln X_{CMC}\right) \quad \text{.....(2)}$$

$$\Delta S°\ \text{m} = (\Delta H°\text{m} - \Delta G°\text{m})/T \quad \text{..... (3)}$$

The d ($\ln X_{CMC}$) dT is the values/slope of the straight line obtained by plotting $\ln X_{CMC}$ against temperature, R is gas constant having the values of 8.314 J/mol and T is the temperature in Kelvin [26].

5.2.5. Calculations of ultrasonic velocity

Using the Digital Ultrasonic Pulse-Echo Velocity meter, the ultrasonic velocities were calculated. The measurement of the velocity is done by the filling of transducer with the solutions then closing the cap of it. Then the cable was connected to the transducer at one end and the velocity meter at the other end. The automatic settings for the velocity meter would display on the meter screen and then recorded the values. The same procedures were carried out for the all the concentration of rutin in different ethanolic concentrations for different temperatures. It is denoted by symbols μ.

Fig. 6: Ultrasonic Sound Velocity Meter

5.2.6. Determination of acoustical parameters

The density and velocity derived from the experiments were used to compute the acoustical parameters. The apparent molar volume and apparent molar compressibility were calculated using the following formulas:

$$\phi_v = \frac{1000}{c}\left\{\frac{\rho_0 - \rho}{\rho_0}\right\} + \frac{M}{\rho_0}$$ …….. Apparent molar volume (1)

$$\phi_k = \frac{1000(\beta - \beta_0)}{c.\rho_0} + \beta.\phi_v$$ …….. Apparent molar compressibility (2)

where, c is the surfactant concentration used, ρ and ρ_0 are the solution and solvent densities, M represents molecular weight of surfactants used, β is the isothermal compression in solution and while β*o* indicates adiabatic compressibility of the solvent [27].

CHAPTER 6

6. Results and discussion

6.1. Density measurement

The densities of rutin trihydrate in hydro-ethanolic mixtures containing the non- ionic surfactant triton X-100 were determined. Even in the context of the various thermodynamic and acoustical investigations of rutin trihydrate, and the triton X- 100 non-ionic surfactant in hydro-ethanolic solutions, density and surface tension depend on molecular interactions and the structures' orientation. The densities were calculated using the specific gravity bottle and weighing balance machine. Densities were calculated for ethanol concentrations of 0% v/v, 10% v/v, 30% v/v, 50% v/v, and 80% v/v for various temperatures of 20℃, 25℃, 30℃, 35℃, and 40℃. Triton X-100 concentrations ranging from 0-0.4mM were generated from stock solutions and densities were calculated for the concentrations of surfactants.

As the concentration of the surfactants increases, their effect depends on the interaction and molecular behavior of the solutions. The densities of the solutions increase when the micelles are formed [28]. At low concentration of the surfactants, its amphiphilic molecules interact with the solvents (ethanol and water) as the concentrations are near to the Critical Micelle Concentration. At these points, micelles usually pack densely leading to the increase in the density. Additionally, surfactants facilitate the solubilization of solutes (rutin trihydrate), further increasing density [29].

Similarly, the density of the solutions stabilizes or decreases beyond the critical micelle concentration (CMC) but in some concentrations of ethanol, the densities increases with the increasing surfactant concentration. When triton X-100 concentration gets beyond the CMC, further molecules instead of forming contacts to the bulk preferentially exist in the micelles. Due to these micelles the overall contribution to density becomes negligible and decrease. However, this applies only for the non-ionic surfactant like triton X-100 [30]

The calculated densities were important for the determination of the surface tension. From this, CMC were calculated and thermodynamics parameters like change in enthalpy, Gibbs free energy and entropy are determined. The density along with ultrasonic velocity was also used in the determination of the acoustical parameters. This is mainly to understand the types of reactions and interactions occurring in the systems, where this helps in understanding the optical concentrations of the solutions for the formulations and drug delivery systems [31].

The calculated densities for 1mM, 2mM, and 3mM of rutin for different ethanol concentrations and for various temperatures are given below in the *table* 1, 2 and 3 respectively.

Table.1: Density (g/cm^3) data obtained by interaction of rutin trihydrate (1mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (1mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	0.945	0.935	0.947	0.940	0.938	1.013	1.001	0.939	0.931	0.931	0.930	0.899	0.899	0.829	0.893	0.875	0.896	0.868	0.873	0.844	0.792	0.782	0.776	0.779	0.764
0.05	0.956	0.939	0.947	0.947	0.947	1.008	1.005	0.941	0.932	0.931	0.930	0.904	0.903	0.898	0.902	0.878	0.901	0.874	0.886	0.847	0.806	0.800	0.783	0.788	0.772
0.1	0.959	0.938	0.949	0.949	0.946	1.061	1.011	0.942	0.929	0.941	0.934	0.911	0.905	0.904	0.903	0.881	0.901	0.880	0.895	0.856	0.820	0.807	0.789	0.789	0.783
0.15	0.958	0.940	0.955	0.941	0.941	1.083	1.013	0.948	0.936	0.939	0.930	0.917	0.910	0.906	0.905	0.884	0.905	0.881	0.904	0.862	0.832	0.814	0.800	0.800	0.783
0.2	0.958	0.946	0.956	0.947	0.948	1.033	1.014	0.948	0.939	0.939	0.932	0.927	0.911	0.908	0.909	0.890	0.906	0.889	0.904	0.865	0.839	0.824	0.813	0.813	0.791
0.25	0.959	0.943	0.961	0.952	0.951	1.023	1.014	0.949	0.941	0.940	0.939	0.920	0.914	0.908	0.913	0.894	0.915	0.890	0.905	0.869	0.838	0.826	0.826	0.817	0.798
0.3	0.959	0.944	0.960	0.952	0.951	1.021	1.021	0.952	0.942	0.940	0.939	0.922	0.916	0.909	0.917	0.890	0.920	0.890	0.909	0.877	0.847	0.835	0.831	0.822	0.813
0.35	0.961	0.943	0.958	0.953	0.9531	1.029	1.018	0.955	0.940	0.942	0.941	0.924	0.916	0.909	0.916	0.895	0.926	0.901	0.916	0.881	0.849	0.848	0.837	0.827	0.821
0.4	0.9670	0.945	0.958	0.955	0.950	1.014	1.020	0.952	0.940	0.936	0.948	0.930	0.920	0.913	0.918	0.900	0.921	0.893	0.910	0.8820.	0.850	0.850	0.842	0.846	0.830

Table.2: Density (g/cm^3) data obtained by interaction of rutin trihydrate (2mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (2mM)																										
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C
0	0.947	0.958	0.940	0.936	0.934	0.933	0.924	0.925	0.928	0.918	0.908	0.908	0.901	0.917	0.904	0.873	0.877	0.857	0.849	0.834	0.799	0.787	0.787	0.787	0.733
0.05	0.962	0.948	0.945	0.929	0.937	0.928	0.929	0.924	0.933	0.919	0.916	0.911	0.907	0.925	0.913	0.881	0.869	0.868	0.852	0.837	0.809	0.792	0.792	0.782	0.781
0.1	0.952	0.955	0.953	0.934	0.935	0.926	0.930	0.932	0.935	0.922	0.917	0.908	0.909	0.917	0.914	0.889	0.874	0.871	0.862	0.846	0.813	0.797	0.804	0.789	0.787
0.15	0.949	0.959	0.953	0.935	0.940	0.921	0.932	0.928	0.932	0.927	0.917	0.912	0.914	0.923	0.919	0.894	0.880	0.880	0.864	0.857	0.830	0.801	0.813	0.798	0.793
0.2	0.961	0.962	0.954	0.935	0.940	0.927	0.931	0.928	0.933	0.928	0.921	0.915	0.917	0.925	0.918	0.894	0.885	0.878	0.874	0.869	0.833	0.808	0.817	0.804	0.797
0.25	0.965	0.962	0.955	0.935	0.948	0.927	0.935	0.935	0.934	0.927	0.918	0.921	0.916	0.926	0.921	0.901	0.890	0.887	0.876	0.868	0.836	0.821	0.821	0.814	0.810
0.3	0.967	0.960	0.956	0.935	0.950	0.930	0.932	0.938	0.933	0.928	0.922	0.915	0.921	0.930	0.925	0.902	0.886	0.882	0.883	0.873	0.850	0.821	0.830	0.822	0.818
0.35	0.967	0.961	0.958	0.937	0.944	0.931	0.931	0.936	0.937	0.933	0.925	0.921	0.927	0.930	0.924	0.900	0.892	0.891	0.887	0.878	0.855	0.822	0.831	0.827	0.822
0.4	0.966	0.961	0.958	0.944	0.949	0.930	0.931	0.938	0.934	0.933	0.928	0.920	0.922	0.933	0.929	0.904	0.897	0.896	0.894	0.885	0.862	0.830	0.835	0.834	0.828

Table.3: Density (g/cm^3) data obtained by interaction of rutin trihydrate (3mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (3mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	0.938	0.942	0.938	0.946	0.939	0.930	0.932	0.935	0.928	0.912	0.922	0.904	0.908	0.899	0.895	0.896	0.855	0.868	0.856	0.854	0.802	0.806	0.804	0.791	0.785
0.05	0.944	0.948	0.946	0.944	0.933	0.932	0.931	0.932	0.933	0.917	0.924	0.917	0.914	0.906	0.889	0.872	0.862	0.872	0.861	0.857	0.819	0.816	0.789	0.795	0.787
0.1	0.949	0.948	0.943	0.955	0.936	0.930	0.938	0.939	0.936	0.914	0.929	0.920	0.917	0.914	0.896	0.879	0.873	0.875	0.870	0.861	0.825	0.822	0.799	0.803	0.796
0.15	0.948	0.946	0.940	0.953	0.937	0.943	0.945	0.933	0.939	0.911	0.925	0.920	0.916	0.913	0.902	0.875	0.876	0.882	0.867	0.828	0.828	0.836	0.813	0.807	0.810
0.2	0.947	0.951	0.937	0.950	0.948	0.939	0.946	0.944	0.941	0.925	0.928	0.916	0.920	0.906	0.911	0.879	0.880	0.886	0.876	0.878	0.830	0.833	0.815	0.813	0.812
0.25	0.948	0.946	0.945	0.954	0.962	0.941	0.943	0.945	0.941	0.931	0.933	0.924	0.920	0.911	0.914	0.889	0.885	0.881	0.878	0.886	0.845	0.833	0.815	0.816	0.830
0.3	0.952	0.950	0.939	0.954	0.945	0.936	0.946	0.945	0.948	0.929	0.932	0.924	0.921	0.914	0.902	0.893	0.895	0.887	0.884	0.884	0.831	0.838	0.816	0.823	0.830
0.35	0.952	0.956	0.887	0.955	0.953	0.947	0.954	0.950	0.945	0.931	0.941	0.932	0.920	0.924	0.918	0.896	0.907	0.898	0.888	0.890	0.845	0.840	0.815	0.828	0.836
0.4	0.955	0.955	0.947	0.950	0.955	0.950	0.949	0.947	0.946	0.935	0.930	0.932	0.922	0.923	0.916	0.905	0.906	0.892	0.890	0.886	0.858	0.849	0.821	0.833	0.848

6.2. Surface Tension

This research evaluated the surface tension properties system containing rutin trihydrate, and triton X-100. The effects of rutin in combination with triton X-100 were observed under 3 different molar concentrations (1-3mM). The surface tension measurements were performed using the pendant drop method using the Attension Theta l tensiometer. Using the Hamilton precision syringe fitted with 22- gauge needle a droplet was formed. Then using charge couple device (CCD) camera the continuous photo of the droplet was taken. The image of the droplet is analyzed using the axisymmetric drop shape analysis (ADSA) method. This method involves analyzing the shape of the droplet to determine its surface properties. The ADSA method utilizes Young- Laplace equation, that describes the capillary pressure differential at the droplet's interface [32] . This equation relates the surface tension to the shape of the droplet based on its curvature. Data processing was carried out by specialized software, such as the Attension software to calculate the surface tension.

Surface tension is measured to find the interaction behavior of rutin trihydrate with triton X-100. This phenomenon is extensively used to evaluate the interactions between solutes and solvents that include non-ionic surfactant. Before being used the tensiometer was calibrated and after calibration the calculated density was added, as it was required for the calculation of surface tension [33]. The measured surface tension of 1mM, 2mM and 3mM concentration of rutin trihydrate at different ethanolic concentration and temperatures are presented below in *table* 4, 5, and 6 respectively. The graphs depicting surface tension in relation to triton X-100 concentration (ranging from 0 to 0.4mM) are shown in *Fig.7-9*. The CMC data were determined from the graph. The CMC values were further converted into mole fraction i.e. X_{cmc}, and these X_{cmc} are useful for the determination of the thermodynamics parameters [34].

Surfactants are known for their ability to reduce surface tension between solutes and solvents within system. The finding shows that an increase in surfactant concentration leads to decrease in surface tension. It is crucial to ensure that the surface tension between solvents, active ingredients, and excipients is minimized to facilitate the formulation’s penetration through cell membranes of affected cells [35]. Therefore, this study suggests administering antioxidant agents like rutin trihydrate with surfactant solution can help overcome the issue of low solubility [36].

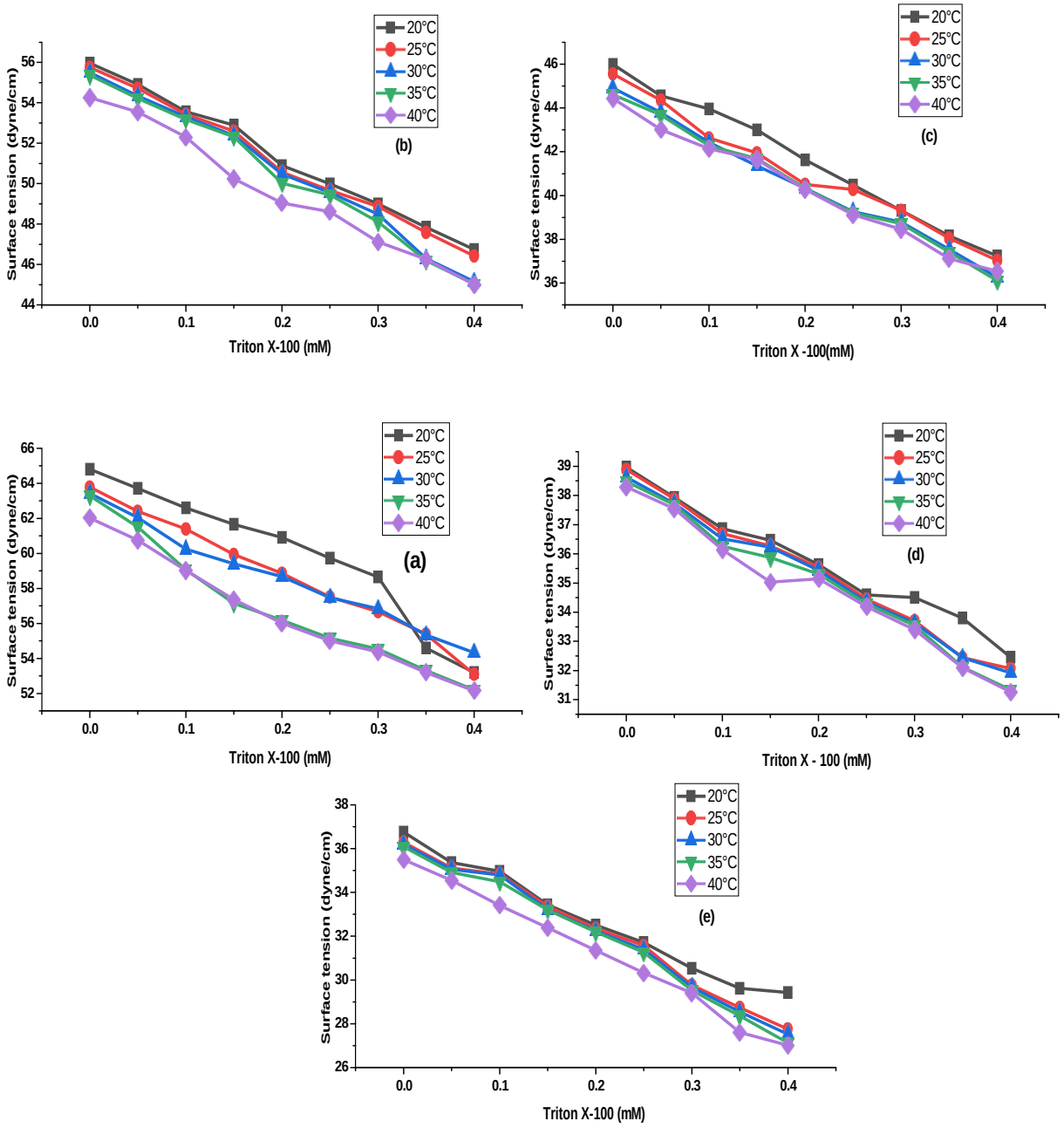


Fig.7: Plot of surface tension vs. Triton X-100 concentrations in different ethanol concentrations: a) 0% v/v ethanol; b) 10% v/v ethanol; c) 30% v/v ethanol; d) 50% v/v ethanol; and e) 80% v/v ethanol for 1 mM rutin trihydrate in various temperatures.

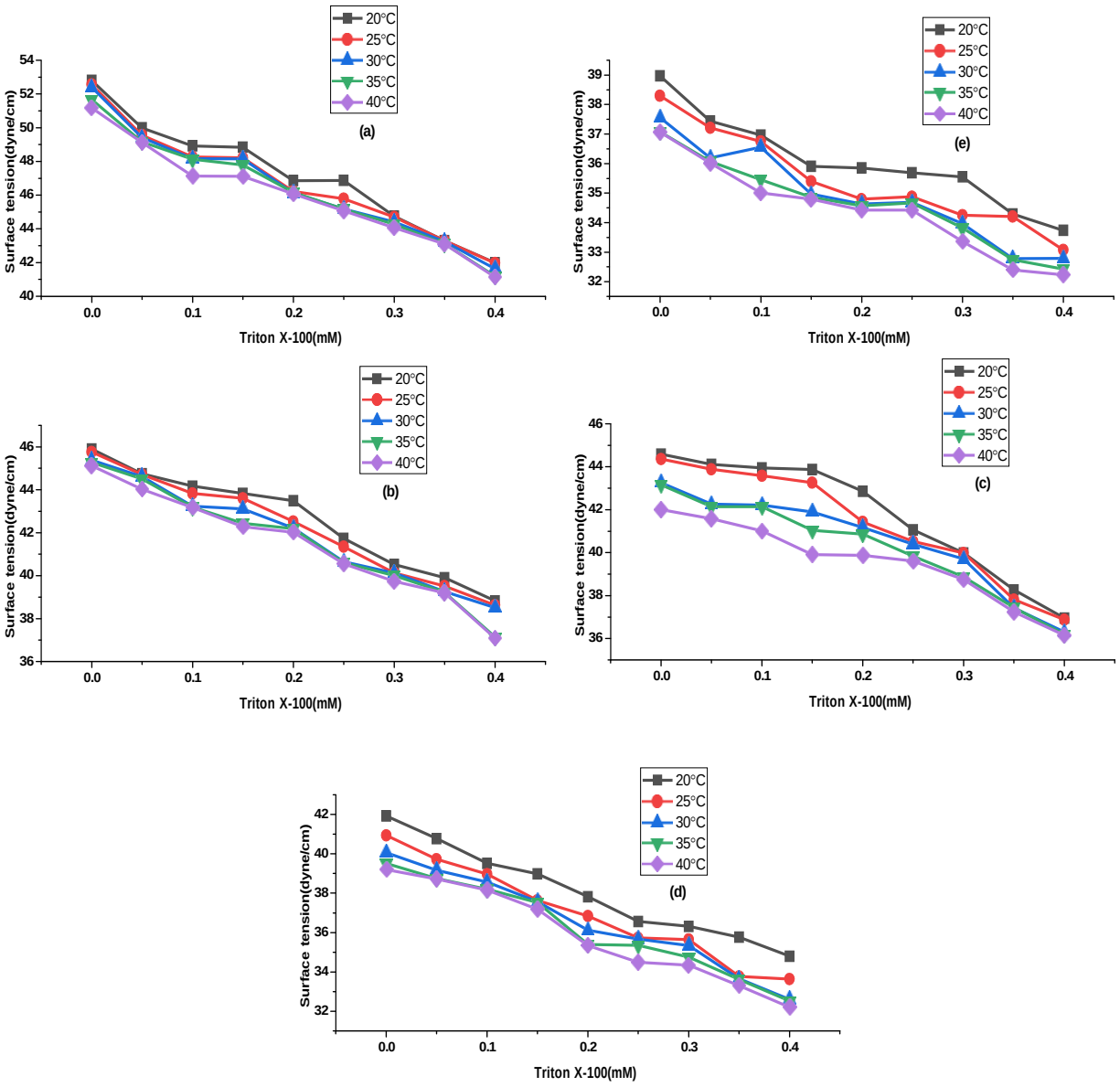


Fig.8: Plot of surface tension vs. Triton X-100 concentrations in different ethanol concentrations: a) 0% v/v ethanol; b) 10% v/v ethanol; c) 30% v/v ethanol; d) 50% v/v ethanol; and e) 80% v/v ethanol for 2 mM rutin trihydrate in various temperatures.

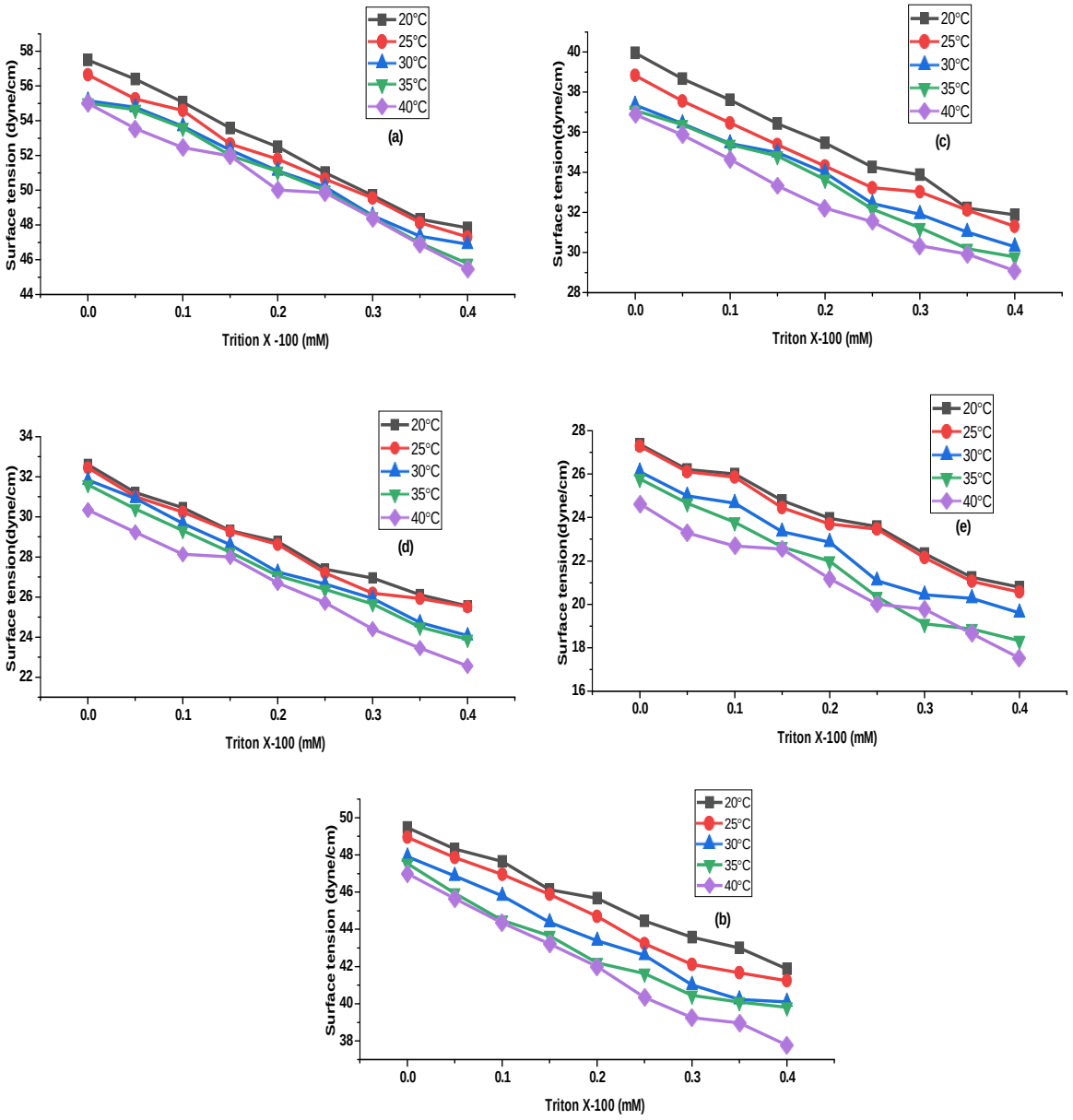


Fig.9: Plot of surface tension vs. Triton X-100 concentrations in different ethanol concentrations: a) 0% v/v ethanol; b) 10% v/v ethanol; c) 30% v/v ethanol; d) 50% v/v ethanol; and e) 80% v/v ethanol for 3 mM rutin trihydrate in various temperatures.

Table.4: Surface tension (dynes/cm) data obtained by interaction of rutin trihydrate (1mM) with triton X-100 (0-0.4mM) indifferent concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (1mM)																										
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	64.808	64.772	63.416	63.28	62.018	56.569	56.149	55.409	55.672	54.246	45.982	45.944	44.908	44.604	44.423	37.965	37.888	37.627	36.974	36.892	36.751	36.284	35.092	35.091	34.494
0.05	62.707	62.39	61.037	61.507	60.745	54.911	54.719	54.342	54.512	53.551	44.55	44.34	44.784	43.679	43.005	36.929	36.876	36.823	36.771	36.542	35.353	35.115	35.061	34.904	33.958
0.1	61.598	61.378	59.236	59.055	59.108	53.558	53.428	53.306	52.871	52.303	42.942	42.619	42.418	42.261	42.133	36.859	36.685	36.609	36.253	36.131	34.965	34.936	34.795	34.387	33.396
0.15	58.662	57.932	57.392	57.148	57.357	52.899	52.591	52.388	50.615	50.241	41.986	41.933	41.343	41.678	41.636	36.466	36.564	36.426	36.169	36.024	34.26	34.365	33.228	33.197	32.384
0.2	57.909	56.856	55.663	54.177	54.012	50.897	50.571	50.276	49.823	49.043	40.624	40.494	40.318	40.319	40.268	35.628	35.525	35.439	35.301	35.134	33.497	33.452	32.742	32.29	32.346
0.25	56.715	56.505	55.462	54.157	54.001	49.982	49.66	49.552	49.446	48.606	40.471	40.262	40.261	40.198	40.121	35.594	35.058	34.552	34.985	34.387	31.708	31.573	31.387	31.249	30.325
0.3	55.65	55.668	53.837	53.537	53.369	49.189	48.866	48.485	48.105	48.112	39.306	39.308	38.779	38.703	38.448	35.502	34.704	34.729	33.541	33.399	30.53	29.776	29.668	29.719	29.708
0.35	54.597	54.38	53.319	53.302	53.182	47.845	47.584	46.299	46.297	46.248	38.149	38.035	37.536	37.403	37.102	34.794	34.437	33.135	33.112	33.986	29.618	28.732	28.549	28.552	27.605
0.4	53.186	53.084	52.326	52.194	52.145	46.743	46.718	45.151	45.126	45.042	37.226	38.022	37.259	36.991	36.536	34.445	34.062	33.119	32.336	32.263	29.414	27.718	27.718	27.128	26.013

Table.5: Surface tension (dynes/cm) data obtained by interaction of rutin trihydrate (2mM) with triton X-100 (0-0.4mM) indifferent concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (2mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	52.797	52.559	52.407	51.674	51.176	45.896	45.762	45.383	45.265	45.122	44.588	44.36	43.252	43.159	42.172	41.921	40.928	40.058	39.517	39.195	38.967	38.293	37.558	37.071	37.065
0.05	49.996	49.565	49.417	49.161	49.124	44.747	44.705	44.615	44.506	44.032	44.545	44.533	42.267	42.154	41.577	40.774	39.719	39.164	38.742	38.724	37.438	37.908	36.193	36.068	36.018
0.1	48.919	48.276	48.167	48.125	47.143	44.162	43.828	43.238	43.186	43.178	43.948	43.274	42.218	42.138	41.132	39.506	38.963	38.56	38.202	38.163	36.964	36.744	36.558	35.452	35.001
0.15	48.838	48.218	48.153	47.794	47.125	43.824	43.598	43.106	42.434	42.278	43.874	43.553	41.901	41.028	39.902	38.981	37.629	37.567	37.525	37.185	35.909	35.392	34.966	34.857	35.795
0.2	46.866	46.227	46.135	46.162	46.083	43.492	42.519	42.215	42.181	42.015	42.855	41.425	41.173	40.859	39.87	37.814	36.833	36.112	35.392	35.333	35.851	34.795	34.632	34.569	34.417
0.25	46.873	45.798	45.182	45.165	45.079	41.736	41.34	40.655	40.608	40.554	41.058	40.521	40.391	39.83	39.609	36.549	35.719	35.667	35.349	34.489	35.687	34.178	34.681	34.664	34.823
0.3	44.752	44.711	44.429	44.276	44.076	40.514	40.128	40.124	39.997	39.743	39.985	39.978	39.701	38.857	38.737	36.309	35.638	35.333	34.754	34.341	35.547	34.25	33.962	33.819	33.365
0.35	43.303	43.299	43.251	43.112	43.109	39.899	39.512	39.263	39.227	39.201	38.264	37.809	37.415	37.43	37.231	35.761	33.765	33.665	33.614	33.296	34.289	34.199	32.781	32.738	32.391
0.4	41.996	41.987	41.648	41.205	41.153	38.822	38.627	38.514	37.137	37.087	36.944	36.875	36.299	36.197	36.137	34.785	33.63	32.603	32.525	32.207	33.738	33.069	32.787	32.422	32.228

Table.6: Surface tension (dynes/cm) data obtained by interaction of rutin trihydrate (3mM) with triton X-100 (0-0.4mM) indifferent concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (3mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35 ℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	55.494	55.644	55.152	55.113	54.998	48.473	47.948	47.907	47.543	46.994	37.956	37.837	37.37	36.992	36.888	31.614	31.449	30.833	29.994	29.343	25.371	25.289	25.113	24.789	24.635
0.05	55.393	55.254	54.782	54.638	54.541	48.326	47.849	46.861	45.738	45.651	36.679	36.564	36.437	36.378	35.874	30.202	30.001	29.918	28.396	28.228	25.208	25.107	25.004	24.659	24.297
0.1	55.059	54.592	53.689	53.589	53.444	47.654	46.951	45.803	44.486	44.337	35.614	35.464	35.445	35.386	34.653	29.456	29.235	28.665	27.31	27.123	24.998	24.864	24.663	23.791	23.685
0.15	53.575	52.652	52.006	52.012	51.973	46.131	45.879	44.38	43.654	43.215	35.435	35.379	34.998	34.815	34.332	29.312	28.873	28.607	27.239	26.994	24.791	24.451	24.353	23.655	23.555
0.2	52.502	51.775	51.112	51.078	51.009	45.661	44.699	43.39	42.212	41.998	34.474	34.321	33.991	33.643	33.225	28.764	27.618	27.236	26.969	26.689	24.069	23.999	23.872	22.989	22.182
0.25	51.012	49.63	50.2	49.986	49.851	44.462	43.232	42.601	41.632	40.337	34.264	34.229	33.447	32.662	31.541	27.391	27.193	26.653	26.378	25.712	23.578	23.475	23.091	22.351	22.007
0.3	49.699	48.641	48.532	48.452	48.394	43.574	42.112	42.005	41.444	40.256	33.892	33.728	32.907	31.237	30.336	26.939	26.193	25.917	25.656	25.392	23.332	22.763	22.446	22.111	21.785
0.35	49.327	47.724	47.345	46.967	46.873	42.997	41.666	41.224	40.089	39.964	32.223	32.12	32.017	31.194	30.023	26.113	26.119	25.121	24.901	24.453	23.241	22.668	22.576	21.877	21.657
0.4	48.029	47.706	46.382	45.771	45.654	41.861	41.437	40.095	39.802	38.768	31.879	31.305	31.295	30.777	29.997	25.547	25.499	24.674	23.887	23.55	22.789	21.767	21.612	21.323	20.526

6.3. Critical micelle concentration

The concentration at which surfactants can form micelles or structures is known as the critical micelle concentration (CMC). When the CMC are dispersed in solvents it is used to establish the concentration of surfactants necessary to create micelles. Micelles are also rounded structures composed of the hydrophobic chains of the surfactants oriented towards the center of the micelle with the polar heads oriented in the outer side towards the water. This property of forming micelles is very useful in drug formulation [37].

In this study, CMC values were obtained by evaluating a surface tension values along with different concentration of the surfactant. The resulting CMC of triton X-100 was nearly constant or increasing with the temperature. For CMC values, two tangents were constructed and the points of intersection of the two lines were considered as CMC. The graph was drawn manually using the graph papers. The rise CMC values have been noticed in this study. The CMC were further converted into mole fraction i.e. X_{cmc} used for the calculation of various thermodynamics parameters such as change in enthalpy (ΔH^o_m), entropy (ΔS^o_m) and Gibb's free energy (ΔG^o_m) of the micellization [38] The *table 7* contains the CMC values of 1-3mM Rutin and different ethanol concentration obtained from the graph;

Table.7: CMC data obtained by interaction of 1-3mM rutin trihydrate with triton X-100 at five different temperatures through surface tension studies

CMC (0% v/v ethanol)				**CMC (10% v/v ethanol)**			**CMC (30% v/v ethanol)**			**CMC (50% v/v ethanol)**			**CMC (80% v/v ethanol)**		
Temp (°C)	**1 mg**	**2 mg**	**3mg**	**1 mg**	**2mg**	**3mg**	**1 mg**	**2mg**	**3mg**	**1 mg**	**2mg**	**3mg**	**1 mg**	**2mg**	**3mg**
20	0.22	0.2	0.24	0.22	0.21	0.25	0.21	0.23	0.23	0.2	0.22	0.24	0.2	0.23	0.26
25	0.23	0.21	0.25	0.23	0.22	0.26	0.22	0.24	0.25	0.23	0.24	0.24	0.22	0.25	0.27
30	0.23	0.23	0.25	0.25	0.22	0.27	0.23	0.25	0.26	0.23	0.25	0.25	0.22	0.25	0.29
35	0.24	0.25	0.27	0.26	0.24	0.27	0.25	0.25	0.27	0.25	0.26	0.27	0.24	0.27	0.29
40	0.26	0.25	0.28	0.26	0.26	0.28	0.26	0.27	0.29	0.25	0.28	0.28	0.25	0.28	0.30

6.4. Thermodynamics parameters determination

The thermodynamics properties of micellization have been determined by converting the CMC values obtained from the surface tension studies into mole fraction units (X_{CMC}). The thermodynamic parameters, including changes in standard entropy (ΔS^{o}_{m}), standard enthalpy (ΔH^{o}_{m}) and Gibbs free energy (ΔG^{o}_{m}) of micellization were calculated using the equations [39];

$$\Delta H°_{m} = -RT^{2} [d (lnX_{CMC})/T] \quad \text{.....(1)}$$

$$\Delta G°_{m} = - RT (lnX_{CMC}). \quad \text{.....(2)}$$

$$\Delta S°_{m} = (\Delta H°_{m} - \Delta G°_{m})/T \quad \text{.....(3)}$$

Here, d ($\ln X_{CMC}$) / dT is straight line slope attained, R represents universal gas constant and T represents temperature of systems [40].

In the *table.8, 9,11 and 12,* the concentrations of 0%v/v, 10%v/v, 30%v/v, 50%v/v and 80%v/v values of X_{CMC} and thermodynamic parameters, namely ΔH^{o}_{m}, ΔS^{o}_{m}, and ΔG^{o}_{m} are given.

The values for ΔH^{o}_{m} are negative for all the concentration of ethanol and the values of ΔG^{o}_{m} are negative in all concentrations whereas, the values of ΔS^{o}_{m} are positive. In this study, micellization is entropically controlled, as indicated by the positive value of ΔS^{o}_{m} [41]. The values progressively drop as the temperature rises when compared to the temperature. The systems' spontaneous reactions are indicated by the negative ΔG^{o}_{m} values. The change in Gibbs free energy is always represented by negative numbers in spontaneous thermodynamic processes. Values get increasingly negative as the system's temperature rises because the spontaneity of the reaction constantly increases.

Furthermore, negative values of ΔH^{o}_{m} confirm that the system's reactions are exothermic. This implies that weak forces mostly control the interactions between solute and solvent molecules, making the system exothermic. Additionally; the research indicates that the interactions between Rutin trihydrate and Triton X -100 are spontaneous as per the values of change in the Gibbs free energy, making them ideal for topical application [42] Positive ΔS^{o}_{m} values show that the process of flavonoid-surfactant complexes transitioning from a dispersed to an aggregating phase is entropically controlled.

Thermodynamic properties for micelles systems with rutin present have been compared in *Fig.10, 11 and 12* represent the plot for ΔG^{o}_{m}, ΔS^{o}_{m} and $\Delta H^{o}_{m,}$ for 1mM, 2mM and 3mM of rutin respectively. In order to improve solubility and permeability of rutin trihydrate within the membranes without compromising its thermodynamic properties, rutin entrapped micelle systems may be useful in pharmaceutical formulations [43]. The positive values of ΔS^{o}_{m} show that the Triton X-100 disrupts the solvent structure doing the micellar formation. It is observed that in all the concentrations of solution the values of ΔG^{o}_{m} were negative which indicate that the reaction in the system is spontaneous in nature. A more spontaneous reaction and a greater likelihood of turning that specific concentration into a topical formulation of drug are associated with more negative values of ΔG^{o}_{m} [44].

Table.8: Thermodynamics parameters for rutin with triton X-100 in 0% ethanol solution at different temperatures.

Rutin Conc.	**T (°C)**	X_{CMC} (10^3)	ΔH^o_m *(kJ mol^{-1})*	ΔG^o_m *(kJ mol^{-1})*	ΔS^o_m *(J mol^{-1} K^{-1})*
1mg	20	0.22	-5.35311	-30.3019	85.149
	25	0.23	-5.53737	-30.7089	84.468
	30	0.23	-5.72475	-31.2241	84.156
	35	0.24	-5.91524	-31.6304	83.491
	40	0.26	-6.10886	-31.9356	82.513
2mg	20	0.2	-8.85048	-30.5341	74.005
	25	0.21	-9.15512	-30.9342	73.084
	30	0.23	-9.46492	-31.2241	71.812
	35	0.25	-9.77987	-31.5258	70.604
	40	0.25	-10.1	-32.0376	70.088
3mg	20	0.24	-5.49586	-30.0899	83.939
	25	0.25	-5.68504	-30.5023	83.279
	30	0.25	-5.87741	-31.0141	82.959
	35	0.27	-6.07298	-31.3288	81.999
	40	0.28	-6.27176	-31.7427	81.377

Table.9: Thermodynamics parameters for rutin with triton X-100 in 10% ethanol solution at different temperatures.

Rutin Conc.	**T (°C)**	X_{CMC} (10^3)	ΔH^o_m *(kJ mol^{-1})*	ΔG^o_m *(kJ mol^{-1})*	ΔS^o_m *(J mol^{-1} K^{-1})*
1mg	20	0.22	-6.49511	-30.3019	81.252
	25	0.23	-6.71868	-30.7089	80.504
	30	0.25	-6.94603	-31.0141	79.432
	35	0.26	-7.17716	-31.4254	78.728
	40	0.26	-7.41208	-31.9356	78.35
2mg	20	0.21	-7.35161	-30.4153	78.716
	25	0.22	-7.60466	-30.8191	77.901
	30	0.22	-7.86199	-31.3362	77.473
	35	0.24	-8.1236	-31.6305	76.321
	40	0.26	-8.3895	-31.9357	75.227
3mg	20	0.25	-3.78287	-29.9905	89.446
	25	0.26	-3.91308	-30.4051	88.899
	30	0.27	-4.04549	-30.8202	88.365
	35	0.27	-4.18011	-31.3288	88.145
	40	0.28	-4.31693	-31.7427	87.622

Table.10: Thermodynamics parameters for rutin with triton X-100 in 30% ethanol solution at different temperatures.

Rutin Conc.	**T (°C)**	X_{CMC} **(10^3)**	ΔH^o_m ***(kJ mol^{-1})***	ΔG^o_m ***(kJ mol^{-1})***	ΔS^o_m ***(J mol^{-1} K^{-1})***
1mg	20	0.21	-7.92261	-30.4152	76.767
	25	0.22	-8.19531	-30.819	75.918
	30	0.23	-8.47263	-31.2241	75.087
	35	0.25	-8.75456	-31.5258	73.933
	40	0.26	-9.04111	-31.9356	73.145
2mg	20	0.23	-5.13899	-30.1936	85.511
	25	0.24	-5.31588	-30.6035	84.858
	30	0.25	-5.49576	-31.0141	84.219
	35	0.25	-5.67863	-31.5259	83.92
	40	0.27	-5.8645	-31.8374	82.98
3mg	20	0.23	-7.70848	-30.1937	76.741
	25	0.25	-7.97382	-30.5024	75.599
	30	0.26	-8.24364	-30.9153	74.824
	35	0.27	-8.51795	-31.3289	74.061
	40	0.29	-8.79675	-31.6515	73.018

Table.11: Thermodynamics parameters for rutin with triton X-100 in 50% ethanol solution at different temperatures.

Rutin Conc.	**T (°C)**	X_{CMC} **(10^3)**	ΔH^o_m ***(kJ mol^{-1})***	ΔG^o_m ***(kJ mol^{-1})***	ΔS^o_m ***(J mol^{-1} K^{-1})***
1mg	20	0.2	-9.77836	-30.5341	70.839
	25	0.23	-10.1149	-30.7089	69.107
	30	0.23	-10.4572	-31.2241	68.538
	35	0.25	-10.8052	-31.5258	67.275
	40	0.25	-11.1588	-31.8373	66.065
2mg	20	0.22	-7.99398	-30.3019	76.136
	25	0.24	-8.26914	-30.6034	74.947
	30	0.25	-8.54896	-31.0141	74.142
	35	0.26	-8.83343	-31.4254	73.351
	40	0.28	-9.12256	-31.7427	72.269
3mg	20	0.24	-6.06686	-30.0899	81.99
	25	0.24	-6.27569	-30.6034	81.637
	30	0.25	-6.48805	-31.0141	80.944
	35	0.27	-6.70394	-31.3288	79.951
	40	0.28	-6.92337	-31.7427	79.295

Table.12: Thermodynamics parameters for rutin with triton X-100 in 80% ethanol solution at different temperatures.

Rutin Conc.	T (°C)	X_{CMC} (10^3)	ΔH^o_m (kJ mol^{-1})	ΔG^o_m (kJ mol^{-1})	ΔS^o_m (J mol^{-1} K^{-1})
1mg	20	0.2	-10.4207	-30.659	69.073
	25	0.22	-10.7794	-31.0551	68.039
	30	0.22	-11.1442	-31.3361	66.64
	35	0.24	-11.515	-31.6304	65.31
	40	0.25	-11.8919	-32.0376	64.363
2mg	20	0.23	-6.70924	-30.1937	80.152
	25	0.25	-6.94017	-30.5024	79.068
	30	0.25	-7.17502	-31.0141	78.677
	35	0.27	-7.41377	-31.3289	77.646
	40	0.28	-7.65643	-31.7428	76.953
3mg	20	0.26	-5.13899	-29.895	84.491
	25	0.27	-5.31588	-30.3116	83.878
	30	0.29	-5.49576	-30.6402	82.985
	35	0.29	-5.67863	-31.1458	82.686
	40	0.30	-5.8645	-31.5632	82.105

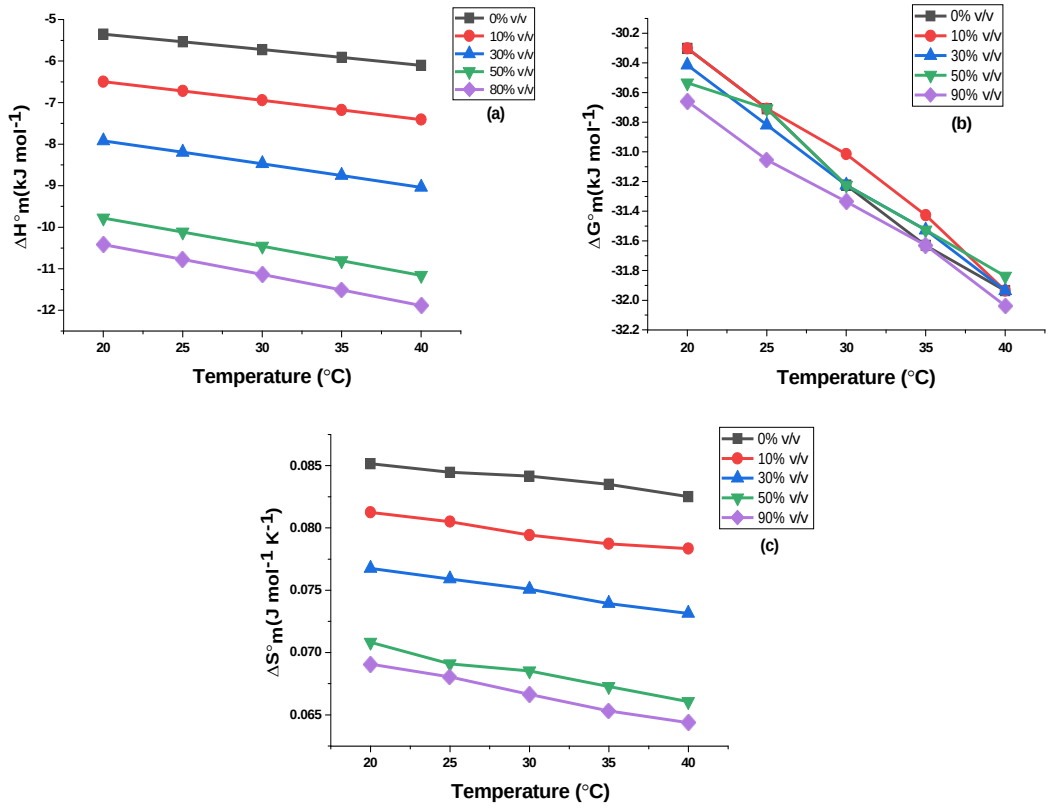


Fig.10: Plots of ΔH^o_m, ΔG^o_m and ΔS^o_m vs. temperature for different ethanolic concentrations of triton X-100 for1mM of rutin.

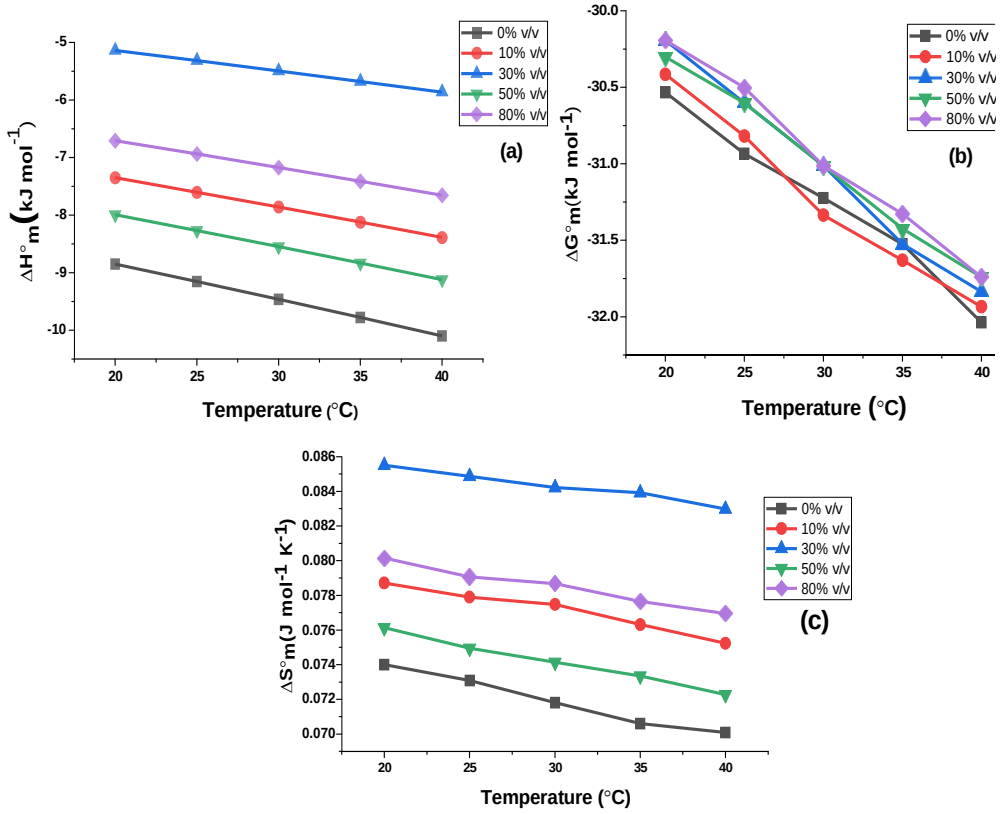


Fig.11: Plots of ΔH^o_m, ΔG^o_m and ΔS^o_m vs. temperature for different ethanolic concentrations of triton X-100 for 2 m M of rutin.

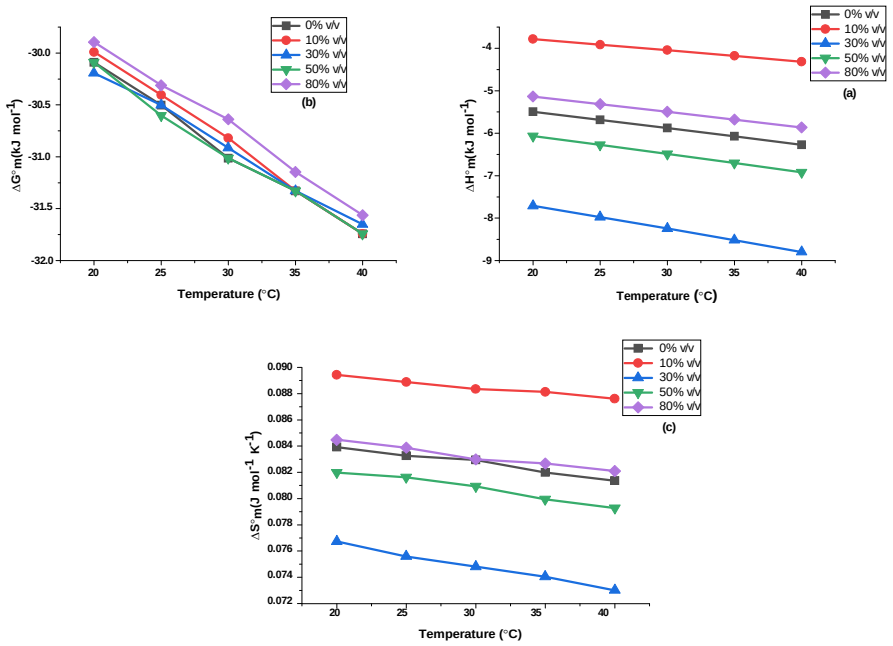


Fig.12: Plots of ΔH^o_m, ΔG^o_m and ΔS^o_m vs. temperature for different hydro-ethanolic concentrations of triton X-100 for 3mM of rutin.

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6.5. Ultrasonic velocity measurement

Velocity measurement offers valuable insights into the interactions between the solute and the solvent in the systems under study. At various temperatures, the ultrasonic sound velocity has been determined for each concentration of surfactants and flavonoids. Various ethanol-water solutions, including 80% v/v, 50% v/v, 30% v/v, 10% v/v, and 0% v/v concentrations, were used for the measurements. It was found that the velocity data was entirely reliant on temperature changes as well as solute and solvent concentrations. Data on ultrasonic sound velocity has been obtained by additional analysis of the flavonoid-surfactant complexes Similar kind of behavior is observed as densities where the ultrasonic sound velocity displaying rise in values during surfactant addition. As the surfactant concentration increases, the velocity values also increases. These rising values demonstrate that there are cohesive forces present, which result in significant intermolecular interactions between surfactants and flavonoids. When determining the interactions in the systems, the temperature and the solute-solvent concentrations are crucial factors, as the data indicates overall [45].

The calculated velocities along with densities of the solutions were used in the determination of the acoustical parameter like apparent molar volume and apparent volume compressibility. This is mainly to understand the types of reactions and interactions occurring in the systems, where this helps in understanding the optical concentrations of the solutions for the formulations and drug delivery systems [46]. The calculated velocities for 1mM, 2mM, and 3mM for different ethanol concentrations and for various temperatures are given below in the *table* 13, 14 and 15 respectively.

Table 13: Ultrasonic velocity (m/s) data obtained by interaction of rutin trihydrate (1mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin Trihydrate (1 mM)																									
Triton 100 (mM)	***0% (v/v) ethanol***					***10% (v/v) ethanol***					***30% (v/v) ethanol***					***50% (v/v) ethanol***					***80% (v/v) ethanol***				
	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C	20°C	25°C	30°C	35°C	40°C
0	1463.50	1474.94	1484.82	1499.58	1490.59	1516.75	1528.03	1531.56	1536.58	1534.92	1598.21	1595.84	1597.07	1588.34	1577.03	1543.26	1513.62	1510.09	1567.97	1571.02	1326.06	1312.23	1311.70	1299.80	1310.76
0.005	1464.05	1475.94	1485.11	1500.37	1491.96	1517.18	1528.66	1532.28	1536.65	1534.28	1598.47	1596.21	1598.28	1588.78	1578.69	1544.27	1514.33	1510.79	1570.25	1571.78	1327.69	1313.66	1312.60	1301.91	1311.53
0.1	1464.71	1476.96	1486.47	1502.37	1493.34	1517.89	1529.94	1532.28	1537.47	1535.19	1599.00	1596.07	1598.84	1589.91	1579.46	1544.73	1515.04	1511.50	1571.78	1572.54	1328.24	1314.77	1312.80	1302.15	1312.60
0.15	1464.99	1478.34	1487.16	1503.76	1494.03	1518.60	1530.66	1533.01	1538.65	1536.67	1599.03	1598.81	1599.21	1589.22	1579.62	1545.47	1517.18	1512.21	1572.54	1573.31	1329.33	1316.29	1313.72	1303.14	1313.66
0.2	1465.91	1479.67	1488.53	1504.46	1495.88	1519.32	1532.99	1534.47	1539.33	1536.92	1599.77	1599.00	1600.02	1590.34	1579.91	1546.21	1517.89	1514.33	1573.34	1574.08	1330.43	1317.74	1315.47	1304.26	1315.07
0.25	1466.21	1480.34	1489.21	1504.76	1496.19	1520.03	1533.01	1535.47	1539.59	1537.05	1600.47	1599.79	1600.27	1590.91	1580.21	1446.95	1518.60	1515.75	1574.08	1575.61	1331.40	1318.49	1316.59	1306.48	1316.14
0.3	1467.97	1481.03	1489.90	1505.16	1497.49	1520.75	1534.15	1535.19	1539.92	1537.45	1600.97	1600.03	1600.92	1591.94	1580.47	1547.69	1519.32	1517.89	1574.84	1576.11	1333.40	1320.74	1318.70	1307.57	1317.26
0.35	1469.02	1481.70	1491.59	1505.99	1499.53	1521.46	1535.19	1535.19	1540.19	1538.03	1600.58	1600.92	1601.48	1592.32	1581.03	1548.43	1520.03	1518.60	1575.61	1577.11	1334.79	1321.82	1319.10	1308.70	1318.18
0.4	1469.49	1482.38	1491.89	1507.03	1499.99	1522.18	1535.94	1535.92	1540.39	1538.92	1601.10	1600.84	1602.05	1592.69	1582.77	1549.18	1520.75	1519.32	1576.38	1577.92	1335.79	1322.995	1320.07	1310.01	1320.16

Table 14: Ultrasonic velocity (m/s) data obtained by interaction of rutin trihydrate (2mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin (2mM)																									
Triton 100 (mM)	***0% (v/v) ethanol***					***10% (v/v) ethanol***					***30% (v/v) ethanol***					***50% (v/v) ethanol***					***80% (v/v) ethanol***				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	1474.94	1480.34	1475.61	1504.56	1510.79	1511.23	1528.12	1537.18	1550.11	1565.22	1581.23	1595.13	1604.11	1616.13	1625.05	1598.12	1602.45	1605.12	1600.12	1589.56	1542.15	1543.12	1542.16	1545.85	1550.06
0.005	1476.96	1481.02	1481.70	1505.15	1511.50	1512.56	1529.33	1538.23	1551.23	1567.89	1581.43	1596.21	1605.33	1617.45	1626.13	1598.75	1603.15	1606.32	1600.95	1590.65	1543.36	1543.65	1542.85	1546.39	1550.89
0.1	1478.31	1484.42	1484.42	1505.54	1512.21	1514.18	1530.16	1539.78	1552.33	1568.13	1582.66	1597.36	1607.56	1618.78	1627.28	1599.13	1604.20	1607.55	1601.35	1591.56	1544.25	1544.21	1543.20	1547.21	1551.09
0.15	1479.67	1486.47	1485.19	1506.57	1513.68	1515.11	1530.89	1540.12	1553.18	1569.54	1583.14	1598.47	1608.18	1619.39	1628.23	1600.05	1605.36	1608.21	1602.49	1592.36	1546.35	1545.62	1543.94	1547.75	1552.30
0.2	1482.38	1487.16	1485.79	1507.27	1514.33	1516.98	1531.55	1540.87	1555.47	1570.11	1584.44	1600.12	1609.34	1620.34	1628.86	1601.20	1606.46	1608.89	1602.87	1593.55	1547.37	1546.54	1544.20	1548.52	1553.40
0.25	1483.06	1487.84	1486.17	1507.97	1515.63	1517.25	1532.23	1541.12	1557.32	1572.36	1585.85	1602.24	1611.21	1621.44	1629.13	1602.23	1607.66	1609.34	1603.45	1594.39	1548.52	1547.41	1545.35	1549.64	1553.79
0.3	1485.11	1488.53	1487.84	1508.68	1516.14	1518.36	1533.45	1542.60	1558.65	1573.82	1586.13	1603.56	1612.38	1622.16	1629.65	1603.15	1608.47	1609.96	1604.10	1595.74	1549.26	1547.93	1546.42	1550.12	1554.32
0.35	1485.79	1489.90	1488.42	1509.38	1517.60	1520.12	1534.50	1543.54	1559.15	1573.25	1587.32	1605.23	1613.45	1623.03	1630.05	1605.34	1609.49	1610.23	1604.85	1596.64	1550.09	1548.59	1547.31	1550.87	1545.26
0.4	1487.84	1491.96	14888.98	1510.09	1518.18	1520.88	1535.13	1545.65	1560.32	1575.23	1588.22	1606.12	1615.12	1624.18	1630.20	1606.12	1610.09	1611.45	1605.29	1598.11	1550.89	1549.03	1547.82	1551.32	1545.23

Table 15: Ultrasonic velocity (m/s) data obtained by interaction of rutin trihydrate (3mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin Trihydrate (3 mM)																									
Triton X 100 (mM)	***0% (v/v) ethanol***					***10% (v/v) ethanol***					***30% (v/v) ethanol***					***50% (v/v) ethanol***					***80% (v/v) ethanol***				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0	1478 .56	1484 .23	1490 .56	1492 .33	1505 .38	1513 .12	1515 .66	1520 .15	1530 .23	1541 .26	1545 .32	1549 .32	1553 .14	1560 .54	1565 .23	1572 .36	1586 .34	1592 .46	1602 .22	1610 .23	1620 .24	1634 .25	1642 .12	1652 .26	1662 .35
0.005	1478 .99	1485 .47	1491 .41	1492 .79	1506 .13	1514 .65	1517 .23	1521 .56	1532 .45	1542 .17	1546 .47	1550 .47	1554 .62	1560 .11	1566 .23	1573 .25	1587 .23	1594 .44	1604 .65	1612 .45	1621 .34	1635 .56	1643 .24	1654 .03	1663 .72
0.1	1480 .54	1486 .29	1492 .13	1493 .52	1507 .03	1515 .12	1518 .34	1522 .58	1534 .28	1543 .54	1547 .11	1551 .27	1556 .54	1562 .23	1567 .45	1574 .38	1589 .12	1596 .32	1605 .56	1613 .95	1623 .65	1636 .49	1644 .56	1655 .87	1664 .16
0.15	1481 .84	1487 .34	1493 .65	1494 .64	1507 .86	1516 .35	1519 .05	1523 .47	1535 .46	1544 .18	1548 .25	1552 .38	1557 .49	1563 .14	1568 .23	1575 .52	1591 .21	1598 .23	1607 .25	1615 .06	1628 .31	1638 .09	1645 .13	1656 .23	1665 .25
0.2	1482 .35	1488 .65	1494 .06	1495 .21	1508 .19	1517 .83	1521 .65	1524 .50	1536 .15	1546 .08	1549 .23	1553 .45	1558 .65	1564 .24	1569 .20	1576 .13	1592 .45	1600 .03	1608 .87	1617 .54	1630 .45	1640 .21	1647 .24	1657 .65	1667 .12
0.25	1483 .13	1489 .28	1494 .58	1496 .33	1509 .25	1519 .06	1522 .11	1525 .16	1537 .25	1547 .19	1550 .46	1554 .13	1559 .13	1565 .85	1570 .12	1578 .46	1594 .35	1601 .45	1610 .23	1618 .45	1632 .74	1642 .34	1648 .32	1658 .32	1668 .32
0.3	1483 .43	1490 .13	1495 .16	1497 .49	1510 .38	1519 .88	1523 .14	1526 .78	1538 .54	1548 .27	1551 .65	1555 .52	1560 .45	1566 .28	1572 .24	1580 .14	1595 .44	1603 .25	1612 .65	1619 .78	1634 .54	1644 .35	1650 .24	1660 .08	1669 .56
0.35	1484 .22	1490 .85	1496 .23	1498 .23	1511 .45	1520 .11	1524 .45	1527 .65	1539 .46	1550 .09	1552 .47	1556 .34	1561 .38	1567 .48	1574 .64	1582 .23	1596 .89	1604 .86	1614 .34	1620 .21	1635 .41	1646 .34	1652 .34	1662 .45	1670 .35
0.4	1485 .56	1491 .25	1496 .85	1499 .09	1512 .86	1520 .96	1525 .53	1528 .95	1540 .21	1552 .14	1553 .58	1558 .13	1561 .13	1568 .52	1575 .16	1583 .84	1597 .46	1605 .91	1616 .42	1621 .41	1638 .21	1648 .65	1654 .45	1663 .95	1672 .35

6.6. *Acoustical parameters*

The apparent molar compressibility (ϕ_k) and volumetric (ϕ_v) parameters have been measured in order to examine the acoustic characteristics of micelle solutions. Understanding these factors yields useful details about different system interactions [47]. *Figures 13–15* show the graphs that were produced for values of ϕ_v in relation to the addition of surfactants in various ethanol concentrations at various temperatures. The values of ϕ_v obtained for surfactant with rutin at different water-ethanol solvent concentrations and temperatures are shown in *Tables 16-18*. Similarly, the plots for values of ϕ_k *vs.* surfactant containing ethanolic concentrations at various temperatures are shown in *Figures 16-18,* while the values obtained by rutin trihydrate interactions with triton X-100 at all concentrations as well as temperatures are represented in *Tables 19-21.*

Understanding these acoustic parameters (ϕ_v and ϕ_k) gives important insights into the interactions taking place in a solution. The addition of surfactants into solutions with flavonoids, rutin trihydrate enhances the rate of micelle formation in ethanol-rich solvent systems. As the solution is hydrophobic-friendly, the inclusion of surfactant appears to create micelle aggregates in the hydrophobic domain of the solution. Additionally, when experiments are conducted in mixed hydro-ethanol, the positive results have been recorded at all concentrations and temperatures investigated. Along with this, a specific trend in data has been noticed where the values are found to be decreasing continuously with addition of surfactant to the solution. Therefore, the acoustical properties give very useful information regarding the interactions of molecules in the solutions which is required for topical formulation [48].

As observed in the graphs, the values for ϕ_v and ϕ_k are reducing in addition of surfactant. Since surfactants employed in the research contain long hydrocarbon chains, their incorporation into the solution influences the intermolecular forces in the solution, thereby weakening them and reducing the values of ϕ_v. Besides this, the incorporation of lipophilic flavonoids into the solution also contributed to increasing the hydrophobicity resulting in reduction of values of ϕ_v and ϕ_k. Also, a reduction in the values up to the value of micellization (CMC values) further indicates that the pre-micellar phase properties are influenced by surfactants. Once micellization has taken place, surfactant influences none of the properties of solution such that ϕ_v values remain independent of the surfactant concentration [49].

The nature of the interactions between the solute and solvent molecules as well as between the solute and the solvent was also revealed by the investigation of apparent molar compressibility and volumetric data. The molecules in the original solution, which contained hydro-ethanolic concentrations and flavonoids, seem to interact electro statically. The use of surfactants caused micellization, which led to molecular aggregation. Micelle creation and further surfactant additions improve the system's hydrophobic interactions, making them dominant at higher surfactant concentrations [50]. The nature of interactions is also influenced by the presence of hydroxyl groups (-OH) in the structures of ethanol and rutin trihydrate. Although these hydroxyl groups are typically hydrophilic, they act as hydrophobic and increase the hydrophobic contacts since they are a part of big hydro-carbon lipophilic moieties in flavonoid structures. Because of the hydrocarbon chain, ethanol's hydroxyl groups also take on a hydrophobic character. When surfactant is added, the synergistic impact of flavonoids and ethanol improves the overall hydrophobicity of the solutions being studied [51]. The plots for ϕ_k were found to be in accordance with ϕ_v data, thus validating and supporting both studies in accordance with each other.

The plot for ϕ_k and ϕ_v are shown in the *figures 13-18* and the experimental data of the ϕ_k and ϕ_v are presented in the *tables 16-21*.

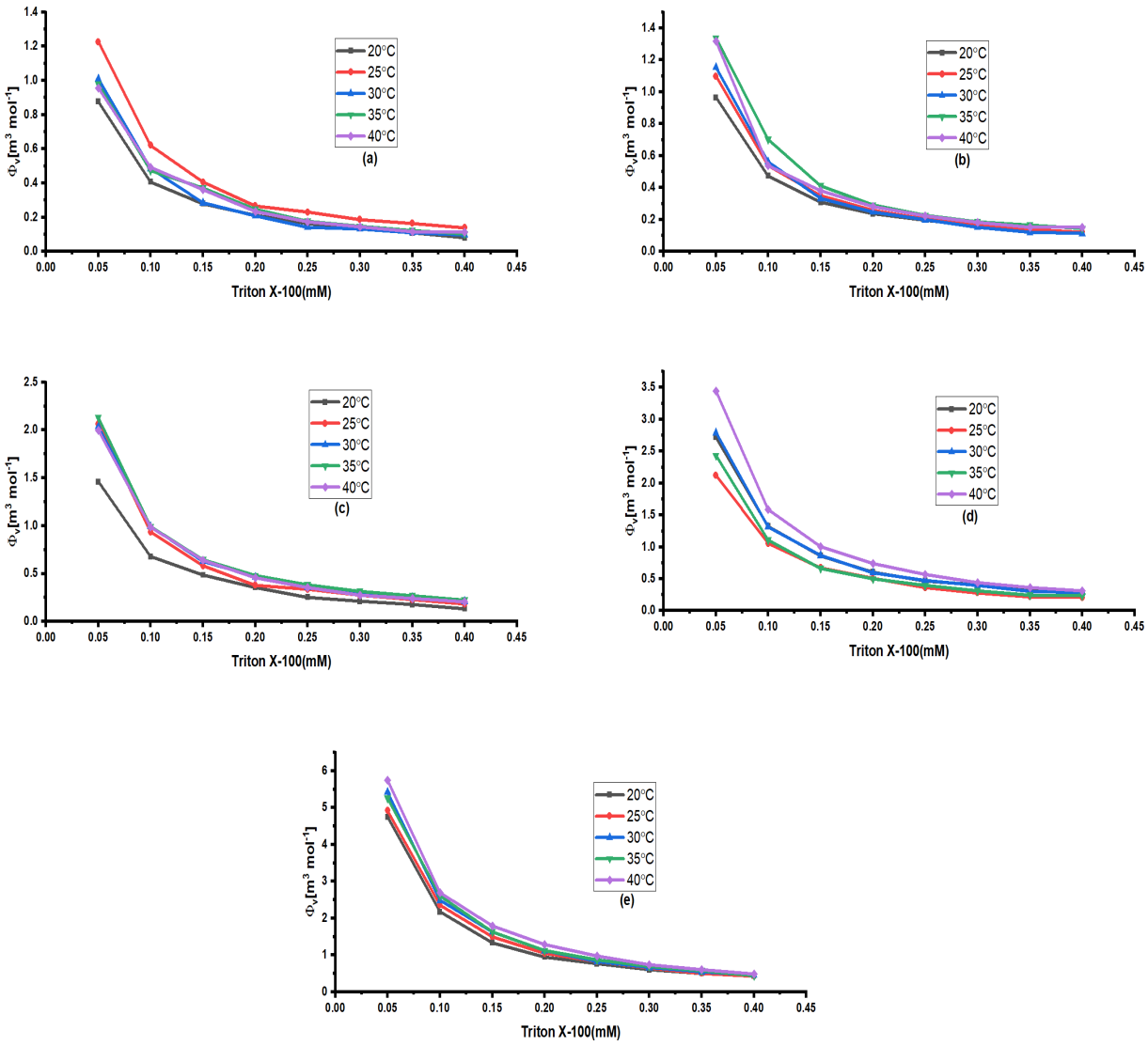

Fig. 13 :Apparent molar volume, ϕ_v (m^3mol^{-1}) vs. triton X-100 for 1mM rutin in different temperatures containing different ethanol concentrations: a) 0% v/v, b) 10% v/v, c) 30% v/v, d) 50% v/v, e) 80% v/v.

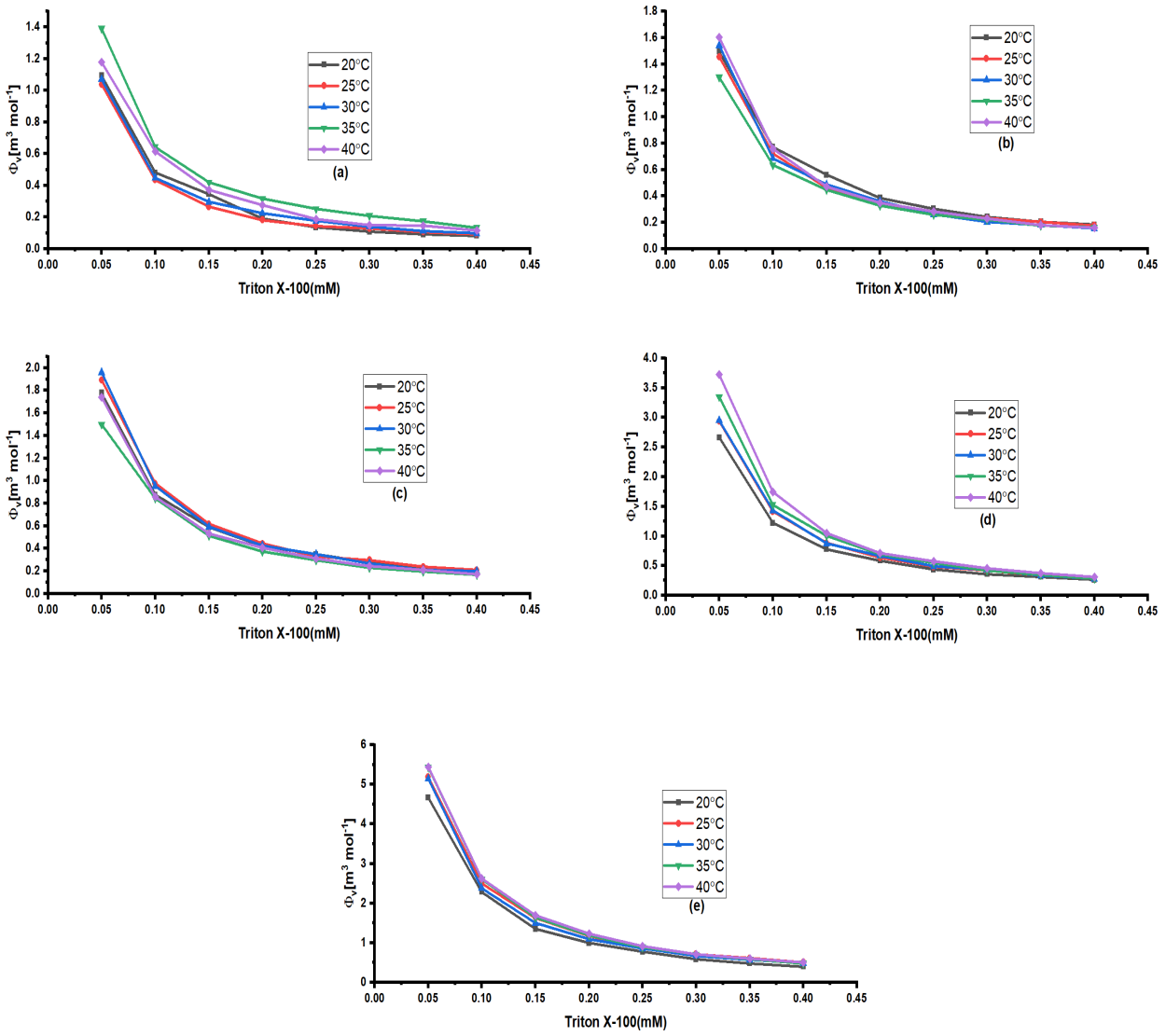

Fig. 14 :Apparent molar volume, ϕ_v (m^3mol^{-1}) vs. triton X-100 for 2mM rutin in different temperatures containing different ethanol concentrations: a) 0% v/v, b) 10% v/v, c) 30% v/v, d) 50% v/v, e) 80% v/v.

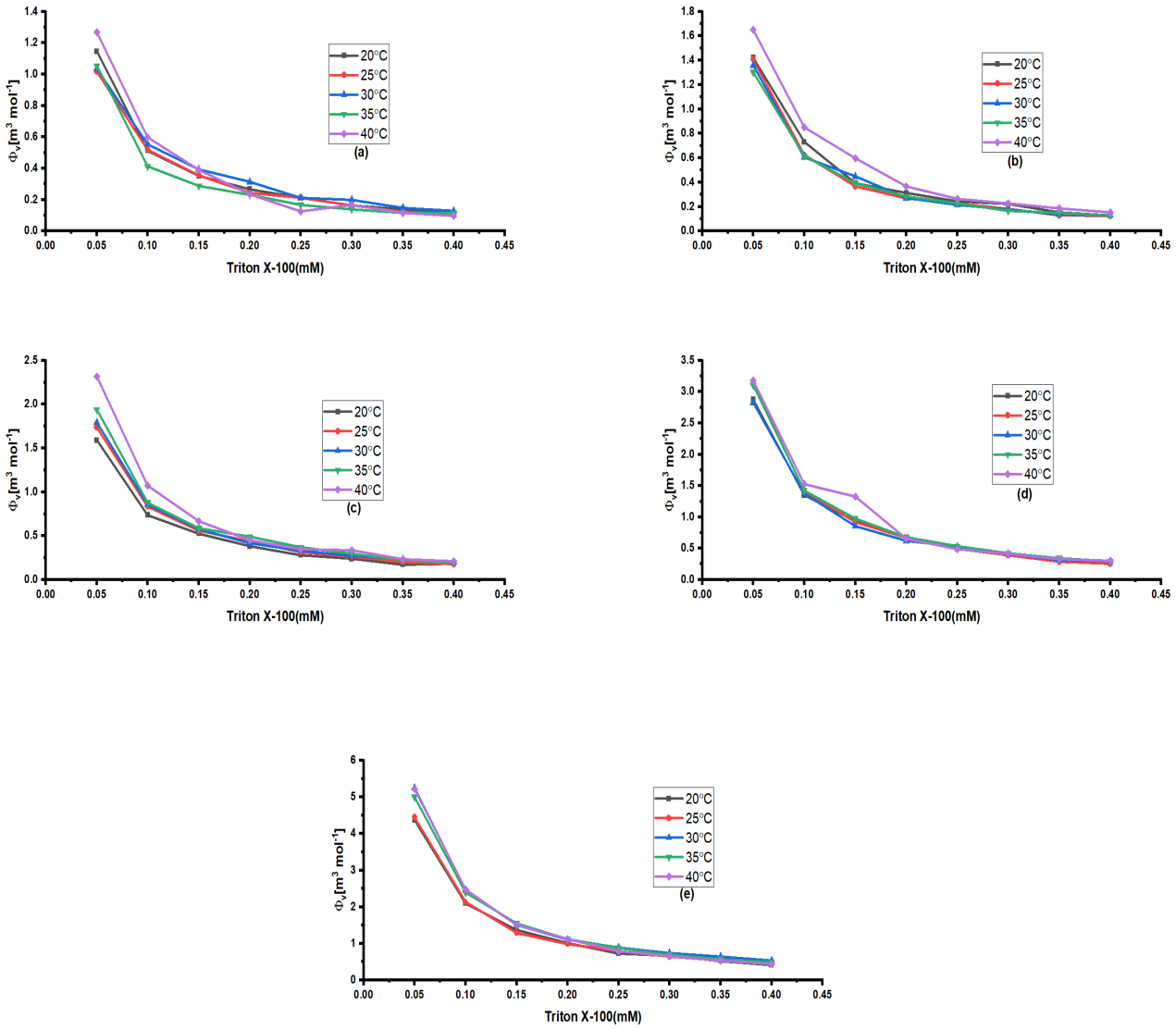

Fig. 15:Apparent molar volume, ϕ_v (m^3mol^{-1}) vs. triton X-100 for 3mM rutin in different temperatures containing different ethanol concentrations: a) 0% v/v, b) 10% v/v, c) 30% v/v, d) 50% v/v, e) 80% v/v.

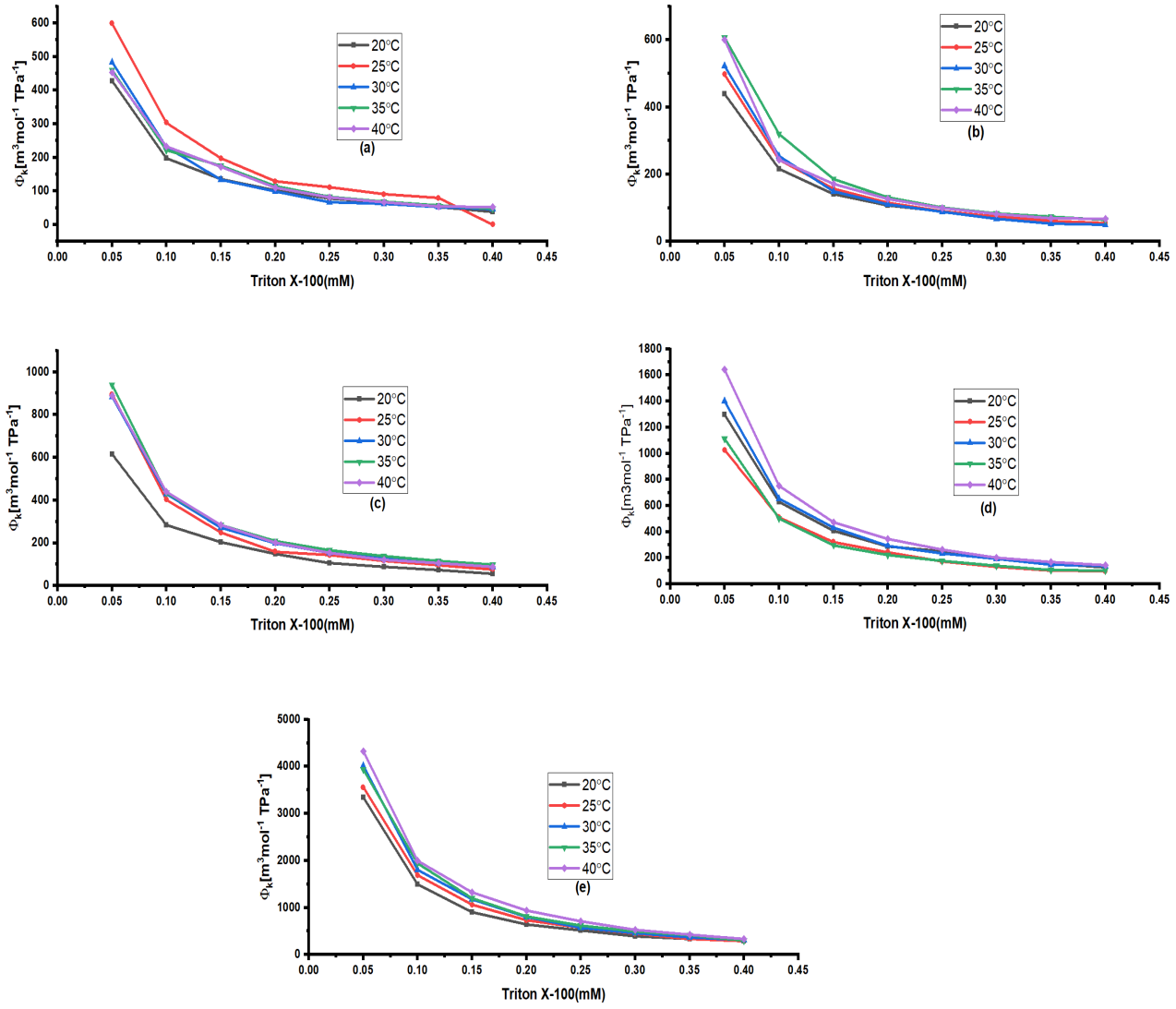

Fig. 16 :Apparent molar compressibility (m^3mol^{-1} TPa^{-1}), ϕ_k vs. triton X-100 for 1mM rutin in different temperatures containing different ethanol concentrations: a) 0% v/v, b) 10% v/v, c) 30% v/v, d) 50% v/v, e) 80% v/v.

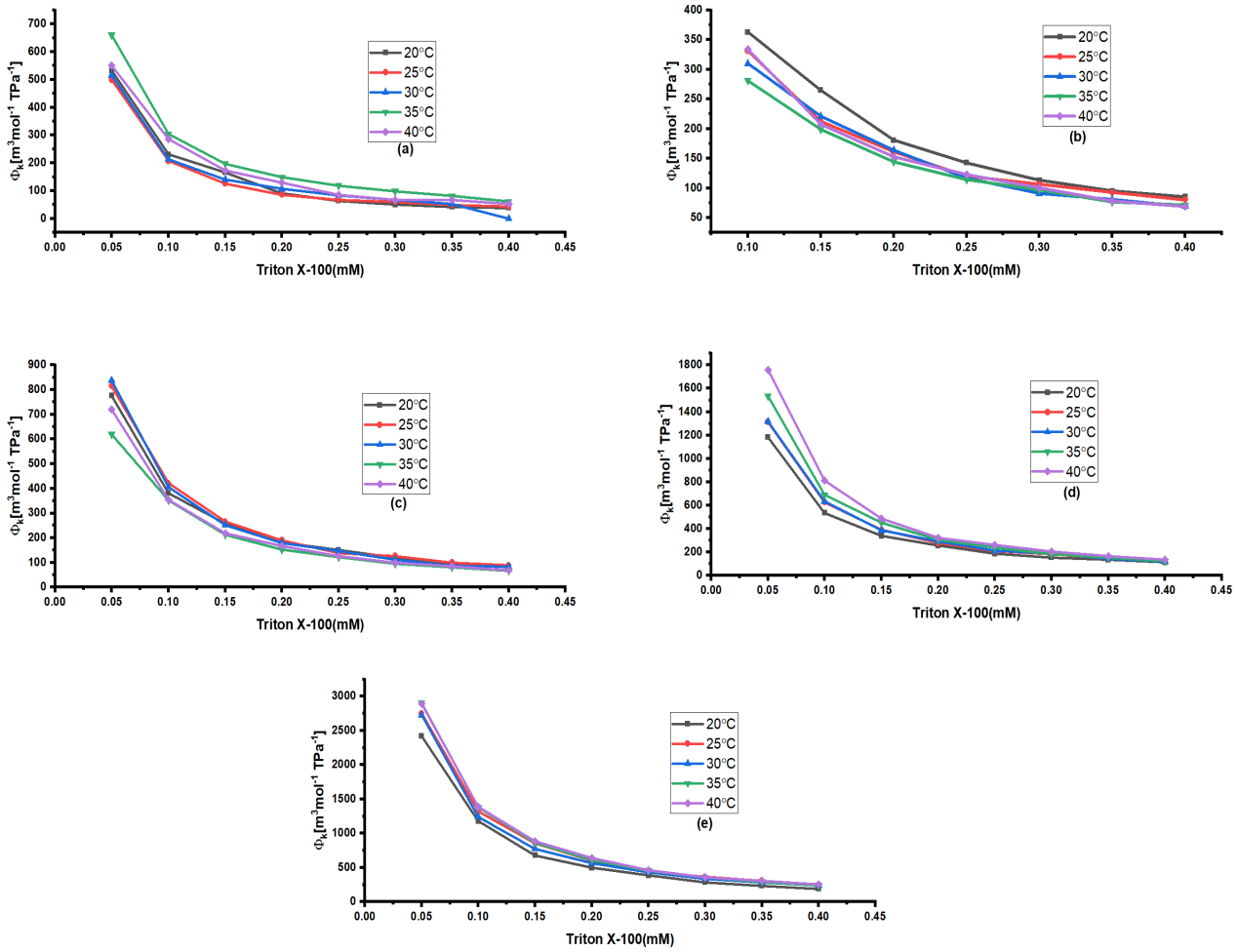

Fig. 17 :Apparent molar compressibility (m^3mol^{-1} TPa^{-1}), ϕ_k vs. triton X-100 for 2mM rutin in different temperatures containing different ethanol concentrations: a) 0% v/v, b) 10% v/v, c) 30% v/v, d) 50% v/v, e) 80% v/v.

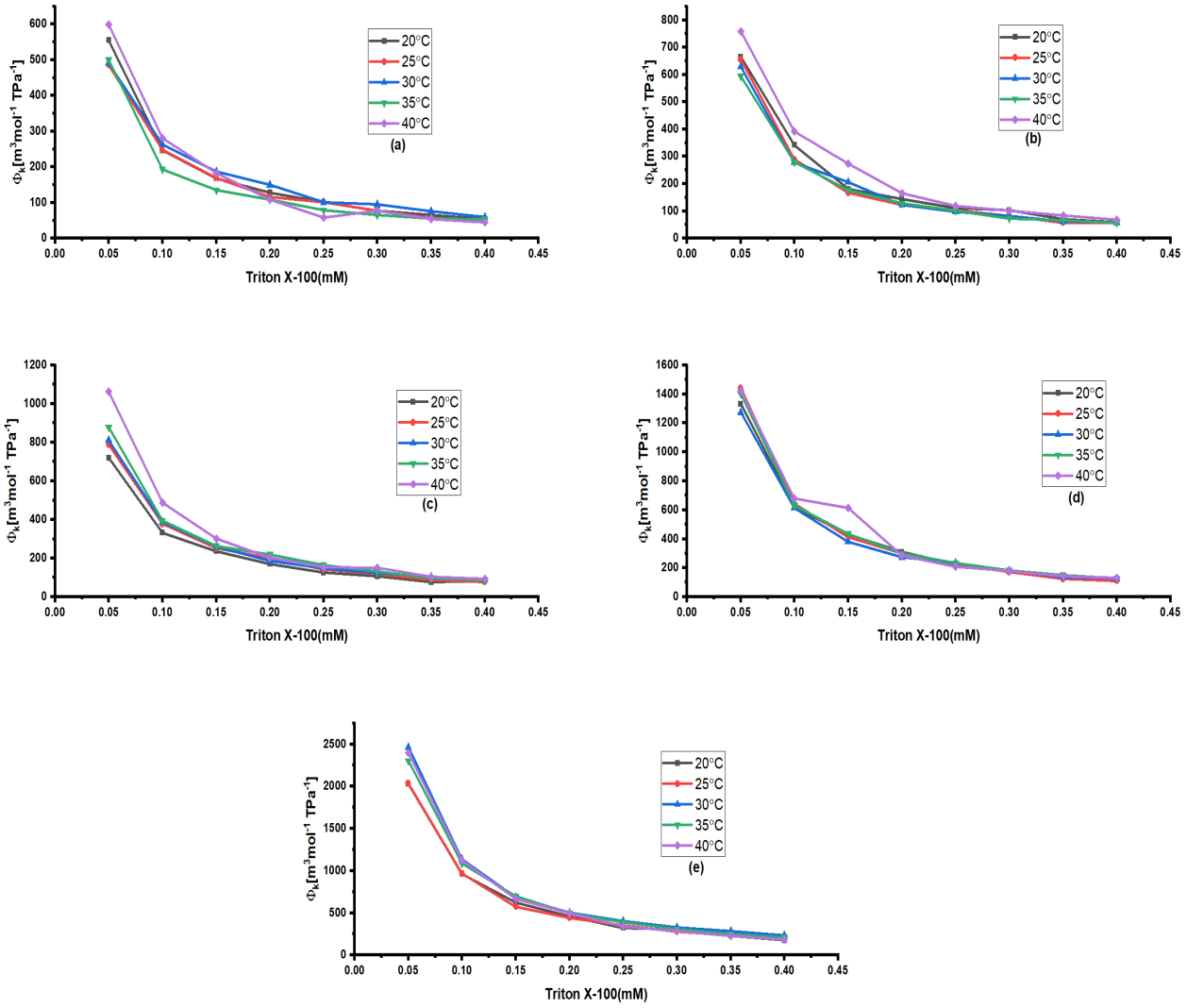

Fig. 18 :Apparent molar compressibility (m^3mol^{-1} TPa^{-1}), ϕ_k vs. triton X-100 for 3mM rutin in different temperatures containing different ethanol concentrations: a) 0% v/v, b) 10% v/v, c) 30% v/v, d) 50%v/v,e)80%v/v

Table 16: Apparent molar volume (m^3mol^{-1}), ϕ_v obtained by interaction of rutin trihydrate (1mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (1mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0.05	0.875	1.226	1.016	0.979	0.956	0.964	1.098	1.153	1.337	1.317	1.460	2.062	2.038	2.129	1.997	2.721	2.123	2.792	2.433	3.442	4.749	4.919	5.425	5.259	5.749
0.1	0.407	0.621	0.485	0.474	0.491	0.473	0.539	0.563	0.703	0.539	0.678	0.935	0.994	0.993	0.989	1.326	1.057	1.314	1.113	1.592	2.173	2.355	2.484	2.601	2.692
0.15	0.278	0.406	0.283	0.372	0.361	0.308	0.348	0.331	0.412	0.379	0.484	0.581	0.629	0.648	0.641	0.862	0.673	0.867	0.666	1.008	1.332	1.494	1.629	1.627	1.788
0.2	0.210	0.266	0.209	0.247	0.233	0.236	0.258	0.248	0.290	0.280	0.353	0.375	0.463	0.477	0.457	0.607	0.504	0.598	0.497	0.738	0.950	1.048	1.122	1.119	1.280
0.25	0.162	0.229	0.142	0.177	0.172	0.197	0.201	0.197	0.225	0.222	0.251	0.332	0.357	0.381	0.349	0.467	0.356	0.475	0.394	0.569	0.762	0.826	0.825	0.867	0.976
0.3	0.134	0.187	0.131	0.147	0.143	0.160	0.165	0.152	0.185	0.183	0.208	0.271	0.290	0.313	0.274	0.405	0.279	0.394	0.313	0.439	0.596	0.648	0.659	0.698	0.738
0.35	0.108	0.164	0.119	0.122	0.116	0.134	0.138	0.119	0.165	0.152	0.173	0.224	0.248	0.266	0.237	0.329	0.219	0.301	0.244	0.362	0.500	0.500	0.542	0.580	0.599
0.4	0.079	0.138	0.097	0.102	0.112	0.114	0.121	0.113	0.142	0.150	0.132	0.180	0.206	0.222	0.202	0.273	0.206	0.287	0.231	0.313	0.437	0.432	0.456	0.438	0.489

Table 17: Apparent molar volume (m^3mol^{-1}), ϕ_v obtained by interaction of rutin trihydrate (2mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (2mM)																									
TritonX-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0.05	1.094	1.037	1.070	1.392	1.179	1.494	1.454	1.541	1.302	1.601	1.779	1.891	1.958	1.500	1.738	2.665	2.935	2.949	3.349	3.721	4.666	5.187	5.148	5.434	5.441
0.1	0.480	0.433	0.448	0.643	0.613	0.771	0.721	0.684	0.633	0.757	0.877	0.978	0.954	0.846	0.859	1.224	1.412	1.431	1.529	1.741	2.282	2.507	2.380	2.608	2.628
0.15	0.345	0.265	0.295	0.419	0.373	0.560	0.464	0.486	0.446	0.472	0.589	0.618	0.593	0.514	0.532	0.773	0.884	0.876	1.002	1.053	1.348	1.629	1.500	1.641	1.688
0.2	0.190	0.181	0.225	0.316	0.277	0.385	0.351	0.361	0.326	0.348	0.420	0.444	0.426	0.371	0.407	0.583	0.631	0.667	0.686	0.709	0.989	1.166	1.096	1.182	1.234
0.25	0.135	0.143	0.176	0.252	0.187	0.304	0.264	0.259	0.258	0.281	0.346	0.328	0.349	0.294	0.308	0.432	0.479	0.487	0.541	0.573	0.772	0.858	0.853	0.888	0.906
0.3	0.107	0.128	0.140	0.209	0.148	0.242	0.232	0.203	0.219	0.230	0.276	0.296	0.268	0.230	0.243	0.357	0.415	0.429	0.421	0.455	0.580	0.714	0.667	0.701	0.711
0.35	0.090	0.105	0.112	0.174	0.144	0.204	0.203	0.180	0.174	0.180	0.225	0.236	0.210	0.196	0.210	0.311	0.337	0.334	0.345	0.375	0.479	0.609	0.569	0.579	0.594
0.4	0.082	0.092	0.097	0.132	0.113	0.183	0.176	0.154	0.161	0.159	0.188	0.208	0.199	0.164	0.170	0.261	0.278	0.277	0.279	0.304	0.394	0.505	0.482	0.482	0.494

Table 18: Apparent molar volume (m^3mol^{-1}), ϕ_v obtained by interaction of rutin trihydrate (3mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (3mM)																										
TritonX-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0.05	1.145	1.016	1.035	1.053	1.268	1.422	1.405	1.358	1.305	1.653	1.591	1.737	1.791	1.937	2.318	2.875	3.130	2.824	3.105	3.176	4.369	4.446	5.254	5.010	5.226
0.1	0.511	0.519	0.553	0.412	0.597	0.730	0.624	0.605	0.615	0.852	0.738	0.835	0.859	0.880	1.072	1.348	1.418	1.373	1.422	1.527	2.095	2.128	2.458	2.387	2.473
0.15	0.350	0.355	0.392	0.287	0.389	0.391	0.364	0.447	0.391	0.595	0.523	0.557	0.577	0.590	0.669	0.934	0.918	0.859	0.976	1.325	1.364	1.287	1.503	1.545	1.502
0.2	0.266	0.243	0.312	0.231	0.233	0.312	0.268	0.271	0.283	0.365	0.379	0.438	0.412	0.486	0.450	0.673	0.666	0.617	0.674	0.649	1.008	0.987	1.108	1.116	1.118
0.25	0.210	0.212	0.212	0.167	0.126	0.242	0.227	0.215	0.224	0.263	0.278	0.314	0.329	0.366	0.344	0.488	0.503	0.522	0.529	0.481	0.727	0.789	0.887	0.873	0.788
0.3	0.162	0.164	0.199	0.139	0.167	0.222	0.180	0.179	0.163	0.227	0.237	0.262	0.273	0.292	0.334	0.391	0.387	0.410	0.418	0.410	0.670	0.633	0.735	0.694	0.653
0.35	0.137	0.121	0.348	0.116	0.116	0.154	0.127	0.138	0.148	0.187	0.172	0.198	0.232	0.218	0.232	0.326	0.284	0.311	0.342	0.328	0.516	0.535	0.634	0.573	0.534
0.4	0.113	0.109	0.128	0.114	0.098	0.127	0.125	0.128	0.127	0.153	0.181	0.174	0.199	0.193	0.208	0.255	0.251	0.290	0.293	0.301	0.407	0.437	0.532	0.483	0.428

Table 19: Apparent molar compressibility (m^3mol^{-1} TPa^{-1}), ϕ_k obtained by interaction of rutin trihydrate (1mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (1mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0.05	427.21	599.21	483.39	458.86	453.40	439.80	497.49	521.94	607.54	601.11	614.35	895.35	882.90	938.39	887.92	1298.31	1027.09	1339.62	1112.97	1644.40	3339.11	3560.01	4016.8	3937.67	4329.3
0.1	197.86	303.46	231.42	221.21	233.12	215.64	243.43	254.57	320.40	242.91	283.73	402.89	429.42	434.15	438.99	630.38	510.82	653.77	503.56	751.33	1501.92	1688.01	1805.8	1942.33	1996.1
0.15	135.43	197.60	134.26	174.6	171.88	140.24	157.13	148.62	185.97	171.30	203.55	247.84	270.64	283.05	283.83	408.42	323.14	430.27	298.26	472.46	906.33	1058.68	1179.4	1198.07	1322.6
0.2	102.12	128.57	99.02	115.60	109.83	107.24	115.81	111.20	130.60	126.51	147.95	158.27	198.55	207.80	201.24	285.30	241.51	293.33	222.15	344.40	640.29	731.82	797.15	808.99	935.48
0.25	78.58	111.18	66.77	82.27	80.90	89.76	90.30	88.46	100.90	99.90	104.49	141.28	152.74	165.81	153.28	249.69	169.98	232.43	175.60	263.63	513.00	574.75	576.39	621.20	705.26
0.3	64.84	90.30	62.04	68.39	67.17	72.85	73.82	67.71	83.07	82.51	86.70	114.91	123.83	136.14	119.75	190.30	131.54	192.01	139.02	201.47	396.19	445.35	455.81	496.11	523.52
0.35	52.22	79.29	51.98	56.75	54.08	60.79	61.79	53.25	74.28	68.55	72.06	94.72	105.53	115.74	103.70	153.30	102.78	145.15	107.59	165.57	330.79	337.45	372.00	410.08	419.64
0.4	37.91	66.72	45.94	47.41	52.48	51.75	54.05	50.47	64.02	68.07	54.39	75.73	87.59	96.06	88.09	126.41	96.89	139.64	102.45	142.88	288.36	290.42	311.20	301.94	338.32

Table 20: Apparent molar compressibility (m^3mol^{-1} TPa^{-1}), ϕ_k obtained by interaction of rutin trihydrate (2mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (2mM)																									
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0.05	531.71	499.42	515.93	660.93	550.54	703.33	668.81	704.72	579.55	708.96	776.16	814.80	837.78	619.78	719.84	1183.46	1313.42	1316.85	1533.47	1756.23	2419.81	2748.27	2728.8	2903.41	2895.8
0.1	231.36	206.97	213.46	303.88	287.04	362.87	331.25	309.93	280.99	333.93	381.70	421.96	406.02	352.09	355.01	538.08	627.76	635.85	691.19	812.72	1177.11	1318.11	1241.9	1380.07	1387.8
0.15	166.48	125.69	140.33	197.3	173.25	264.99	212.76	220.77	198.64	206.94	256.38	265.12	251.11	212.28	218.58	337.76	389.60	384.85	451.59	484.39	678.79	850.99	774.03	857.90	883.43
0.2	90.70	85.53	106.99	149.03	128.58	180.60	160.99	164.01	144.32	152.33	181.80	189.70	179.53	152.83	167.46	254.62	276.45	293.35	305.43	321.38	495.95	602.98	562.83	612.57	641.71
0.25	63.66	67.31	83.76	118.45	85.97	142.39	120.48	116.97	114.12	122.69	149.89	138.81	146.78	120.96	126.20	187.03	208.19	212.10	240.52	259.88	384.96	436.57	435.07	454.48	463.55
0.3	50.58	60.27	66.46	98.27	67.82	113.24	106.18	90.86	96.86	100.22	119.10	126.02	111.85	94.36	99.13	154.10	181.12	187.74	185.22	204.80	284.07	362.83	336.10	354.99	359.63
0.35	42.42	49.66	52.84	81.73	66.58	94.97	92.62	80.83	76.59	78.02	96.80	99.67	87.15	80.07	85.58	134.23	145.81	144.46	151.36	167.63	233.40	309.05	286.01	291.23	302.56
0.4	38.55	43.20	45.89	61.67	52.06	85.10	80.27	69.08	71.16	68.82	80.62	87.85	82.98	66.71	68.94	111.93	119.75	119.28	121.39	134.67	190.67	253.60	241.17	240.04	251.65

Table 21: Apparent molar compressibility (m^3mol^{-1} TPa^{-1}), ϕ_k obtained by interaction of rutin trihydrate (3mM) with triton X-100 (0-0.4mM) in different concentrations of ethanol at various temperatures (20 ℃ to 40 ℃)

Rutin trihydrate (3mM)																										
Triton X-100 (mM)	*0% (v/v) ethanol*					*10% (v/v) ethanol*					*30% (v/v) ethanol*					*50% (v/v) ethanol*					*80% (v/v) ethanol*				
	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃	20℃	25℃	30℃	35℃	40℃
0.05	554.79	485.39	491.62	500.38	598.88	665.34	655.27	629.05	594.51	758.05	719.42	787.56	811.13	878	1062.02	1330.97	1440.83	1272.78	1400.28	1425.26	2028.46	2036.52	2565.72	2301.27	2396.4
0.1	245.85	247.87	263.39	193.59	280.62	342.00	288.55	278.32	279.25	391.14	331.89	377.30	386.60	394.46	486.89	618.35	642.87	615.23	633.71	680.40	926.70	966.47	1136.5	1083.87	1121.1
0.15	168.45	169.84	187.28	135.18	182.62	180.53	167.02	206.80	176.65	274.01	236.02	251.27	259.75	264.62	301.57	429.90	413.58	381.39	435.66	612.89	620.87	573.99	683.15	697.34	668.18
0.2	128.09	115.38	149.38	108.79	108.05	144.54	122.77	123.46	127.10	165.06	170.34	198.04	184.32	219.35	200.75	308.12	298.39	271.89	297.05	282.61	456.59	440.65	500.73	499.58	495.72
0.25	100.77	101.41	100.59	78.22	57.64	111.67	103.92	98.18	101.10	118.11	124.21	140.73	147.17	164.11	153.04	220.56	223.66	231.26	232.33	207.33	322.76	351.20	400.29	388.70	341.35
0.3	77.63	78.02	94.82	65.04	77.79	102.79	82.35	81.43	72.87	102.00	105.62	117.51	122.09	130.30	150.12	175.50	170.38	179.97	181.86	176.72	301.77	279.54	330.75	306.03	282.32
0.35	65.68	57.19	175.47	54.54	53.55	70.46	57.42	62.42	66.43	83.56	75.89	87.90	103.55	96.27	102.00	145.52	122.91	134.65	148.12	140.47	228.37	234.92	285.22	250.53	229.06
0.4	54.01	51.69	60.39	53.78	44.87	57.89	56.75	58.16	56.94	68.25	80.76	77.05	88.88	85.39	91.62	112.46	108.80	126.32	126.06	129.38	176.78	189.74	236.55	209.50	180.78

CHAPTER 7

7. Conclusion

The thermodynamic and acoustical investigations have been studied for triton X-100 in the presence of flavonoids, rutin trihydrate at different hydro-ethanolic concentrations for various temperatures. The surface tension investigations concluded that micellization is impacted by the presence of rutin trihydrate and triton X-100. The results indicate that the surface tension havebeen decreasing when concentration of the surfactant is increased. In addition, increase in the CMC values has been noticed with increase in the temperature. Similarly, the data from the thermodynamics parameters revealed that changed in the enthalpy is negative, whereas the change in the Gibbs free energy is negative in this study. Moreover, change in the entropy determined to be positive. The increase in temperature of the flavonoid-surfactant solutions enhanced the exothermic nature and spontaneity of the reactions. Thus, it shows that rutin-triton X-100 interactions are exothermic and spontaneous in nature and induced entropically regulated reactions. The acoustic studies confirmed the occurrence of electrostatic and hydrophobic interactions between solvents and solute. Although electrostatic molecular interactions existed at lower levels of surfactant, hydrophobic interactions were found to be prevalent in high concentration of surfactant in the solutions. This research work has been found to be highly useful in the design of new and better topical formulations. Thus, understanding these interactions can assist in finding the optimal and viable concentrations of rutin trihydrate, and tritonX-100 for the preparation of drug formulations.

CHAPTER 8

8. References

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