PHYSICO-CHEMICAL STUDIES OF QUERCETIN WITH CATIONIC SURFACTANT CTAB IN HYDRO-ETHANOLIC SOLVENT SYSTEM

Project report submitted in partial fulfillment of the requirement for the degree of

Bachelor of Technology

in

BIOTECHNOLOGY



May 2019

By

Himalya Attri (151803) Diksha Sharma (151816)

Under the guidance of

Dr. Poonam Sharma Assistant Professor (Senior Grade)

Department of Biotechnology and Bioinformatics Jaypee University of Information Technology Waknaghat-173234 Himachal Pradesh

TABLE OF CONTENTS

Chapter No.	Topics	Page No.
	Declaration	iii
	Supervisor's Certificate	iv
	Acknowledgement	v
	List of Figures	vi
	List of Tables	vii
	List of Symbols and acronyms	viii
	Abstract	ix
Chapter-01	Introduction & Review of Literature	1-9
	1.1 Introduction	
	1.2 Review/Background Material	
	1.3 Objectives	
Chapter-02	2.1 Materials/Equipments used	10-11
	2.1.1 Temperature Control and Thermostat	
	2.1.2 Conductivity Meter	
	2.1.3 Viscometer	
	2.1.4 Ultrasonic Velocity Meter	
	2.2 Methodology	12-13
	2.2.1 Conductance Measurement	
	2.2.2 Thermodynamic Parameters	
	2.2.3 Density and Ultrasonic sound Velocity	
	Measurements	

	2.2.4 Relative Viscosity Measurements	
	2.2.5 Apparent Molar Volume and Molar Adiabatic	
	Compressibility	
Chapter-03	Results and Discussion	14-30
	3.1 Conductivity Studies	
	3.2 Thermodynamic Parameters	
	3.3 Viscosity Studies	
	3.4 Ultrasonic Sound Velocity Studies	
Chapter-04	Conclusion	31-32
Chapter-05	References	33-37

DECLARATION

We hereby declare that the project titled **"Physico-chemical studies of Quercetin with cationic surfactant CTAB in hydro-ethanolic solvent system"** is submitted as Project Work carried out by us at Jaypee University of Information Technology, Solan under the guidance of **Dr. Poonam Sharma**. Any further extension, continuation or use of this project has to be undertaken with prior express written consent from the Supervisor, Jaypee University of Information Technology, Solan-173234.

We further declare that the project work or any part thereof has not been previously submitted for any degree or diploma in any university.

Signature of Student

Name: Himalya Attri

Date :

Signature of Student

Name: Diksha Sharma

SUPERVISOR'S CERTIFICATE

This is to certify that the work titled "Physico-chemical studies of Quercetin with cationic surfactant CTAB in hydro-ethanolic solvent system" submitted by "Himalya Attri (151803) and Diksha Sharma (151816)" in partial fulfilment for the award of Degree of Bachelor of Technology in Biotechnology of Jaypee University of Information Technology, Waknaghat has been carried out under my supervision. This work has not been partially or wholly submitted to any other University or Institute for the award of this or any other degree or diploma.

Signature of Supervisor	
Name of Supervisor	Dr. Poonam Sharma
Designation	Assistant Professor (Senior Grade)
Date:	

ACKNOWLEDGEMENT

"Every great achiever is inspired by a great mentor". This acknowledgement is a profound expression of regard for all those who have made this work indelible.

We are highly indebted to **Dr. Sudhir Kumar**, Head, Department of Biotechnology and Bioinformatics for giving us the golden opportunity and amenities required to carry out our project successfully.

We would like to thank our teacher **Dr. Poonam Sharma**, for giving us the opportunity to work for our final year project. We were provided with all the apparatus and materials our project required and we are highly grateful for that.

We would also like to thank our Ph.D scholar Mr. Vikrant Abbot and lab assistants Mr. Ismail and Mrs. Mamta for their constant and selfless support towards us to partially complete the project to the best of our efficiencies.

We bow our head before the **Almighty God** whose blessing gave us the strength to make this successful venture and We dedicate our work and achievement in his lotus feet.

Thank you!

Signature of Student

•••••

•••••

Name of the Student

Himalya Attri

Diksha Sharma

Date :

List of Figures

Title	Page no.
Classification of Polyphenols	2
Health Benefits of Quercetin	6
Structure of Cationic Surfactant CTAB	8
Variation of Specific Conductance (κ) with concentration	
of CTAB at different temperature in 1mM Quercetin	15
Variation of Specific Conductance (κ) with concentration	
of CTAB at different temperature in 2mM Quercetin	16
Variation of Specific Conductance (κ) with concentration	
of CTAB at different temperature in 3mM Quercetin	16
Graphical representation of Change in Enthalpy (ΔH^o_m) vs.	
Temperature for different concentrations of QC (1-3mM)	
in aqueous solution	21
Graphical representation of Change in Entropy (ΔS°_{m}) vs.	
Temperature for different concentrations of QC (1-3mM)	
in 30% v/v Ethanol solution	21
Graphical representation of Change in Gibbs free energy	
(ΔG°_{m}) vs. Temperature for different concentrations of QC	
(1-3mM) in 70% v/v Ethanol solution	22
Graph representing apparent molar volume (ϕ_v) vs. CTAB	
concentration in 70% v/v ethanol solution containing 1mM	
Quercetin at different temperatures	29
Graph representing apparent adiabatic compressibility (ϕ_k)	
vs. CTAB concentration in 100% v/v ethanol solution	
containing 1mM Quercetin at different temperatures	29
	 Classification of Polyphenols Health Benefits of Quercetin Structure of Cationic Surfactant CTAB Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 1mM Quercetin Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 2mM Quercetin Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 3mM Quercetin Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 3mM Quercetin Graphical representation of Change in Enthalpy (ΔH°_m) vs. Temperature for different concentrations of QC (1-3mM) in aqueous solution Graphical representation of Change in Entropy (ΔS°_m) vs. Temperature for different concentrations of QC (1-3mM) in 30% v/v Ethanol solution Graphical representation of Change in Gibbs free energy (ΔG°_m) vs. Temperature for different concentrations of QC (1-3mM) in 70% v/v Ethanol solution Graph representing apparent molar volume (Φ_v) vs. CTAB concentration in 70% v/v ethanol solution containing 1mM Quercetin at different temperatures Graph representing apparent adiabatic compressibility (Φ_k) vs. CTAB concentration in 100% v/v ethanol solution

List of Tables

Table no.	Title	Page no.
1.	CMC data obtained by interaction of Quercetin (1-3 mM)	
	with different concentrations of CTAB at temperatures	
	(20-40 °C)	15
2.	Thermodynamic parameters for different concentrations of	
	Quercetin (1-3 mM) in pure water at different temperatures	
	(20-40 °C)	17
3.	Thermodynamic parameters for different concentrations of	
	Quercetin (1-3 mM) in 30% EtOH at different temperatures	
	(20-40 °C)	18
4.	Thermodynamic parameters for different concentrations of	
	Quercetin (1-3 mM) in 70% EtOH at different temperatures	
	(20-40 °C)	19
5.	Thermodynamic parameters for different concentrations of	
	Quercetin (1-3 mM) in 100% EtOH at different temperatures	
	(20-40 °C)	20
6.	Density, ρ (g cm ⁻³) obtained by interaction of Quercetin (1-	
	3 mM) with different concentrations of CTAB (0.5-1.77mM)	
	and ethanol at five different temperatures	24
7.	Ultrasonic sound velocity, μ (m s ⁻¹) obtained by interaction	
	of Quecetin (1-3 mM) with different concentrations of CTAB	
	(0.5-1.77mM) and ethanol at five different temperatures	25
8.	Relative viscosity, η_r (centipoise) obtained by interaction of	
	Quercetin (1-3 mM) with different concentrations of CTAB	
	(0.5-1.77 mM) and ethanol at five different temperatures	26
9.	Apparent molar volume, ϕ_{ν} (m ³ mol ⁻¹) for Quercetin (1-3 mM)	
	with different concentrations of CTAB (0.5-1.77 mM) and	
	water-ethanol at five different temperatures	27
10.	Apparent adiabatic compressibility, ϕ_k (m ³ mol ⁻¹ TPa ⁻¹) for	
	Quercetin (1-3 mM) with different concentrations of CTAB	
	(0.5-1.77 mM) and water-ethanol at five different temperatures	28

List of Symbols and Acronyms

CTAB	Cetyltrimethyl Ammonium Bromide
QC	Quercetin
EtOH	Ethanol
к	Specific Conductance
СМС	Critical Micelle Concentration
ή	Viscosity Co-efficient
ή _r	Relative Viscosity
$\Delta H^{\circ}{}_{m}$	Standard Enthalpy Change
ΔS_{m}°	Standard Entropy Change
ΔG°_{m}	Standard Gibbs Free Energy Change
$\Phi_{\mathbf{v}}$	Apparent Molar Volume
Φ_k	Apparent Molar Compressibility

<u>Abstract</u>

Flavonoids are very well known for its use in pharmaceutical industry possessing various health benefits that can be utilised for tackling the problem of numerous health related diseases. Quercetin, a flavonoid possesses greater health benefits but its use is limited due to various insolubility and instability problems and thus, is taken into consideration. Thermodynamic and thermoacoustic properties of Quercetin at different concentration have been studied in interaction with CTAB surfactant in varied hydro-ethanolic concentrations at different temperatures. The conductivity of the overall system has been studied and further, it has been utilised to calculate Change in Enthalpy (Δ H), Entropy (Δ S) and Gibbs free Energy (ΔG) of micellization. The study revealed that though the interactions between Quercetin and CTAB are endothermic in nature, the reaction spontaneously proceeds in forward direction. Further, density and ultrasonic sound velocity parameters have been used to calculate the thermoacoustic parameters i.e. apparent molar volume and apparent adiabatic compressibility. Thermoacoustic properties revealed the dominance of hydrophobic interactions at higher surfactant concentration. The data has been found to be more favourable in hydro-ethanolic solution as compared to that of aqueous solution. Overall, the interactions are favourable for the system to be utilised for formulation development studies, drug development, medical administration, drug industry and pharmaceutical industries

CHAPTER-01

INTRODUCTION

AND

REVIEW OF LITERATURE

1.1 Introduction:

Plants and its parts are used for its scent, flavour or therapeutic properties. There are number of advantages associated with using plants and its phytoconstituents in pharmaceutical products. Plants have the capacity to synthesize different organic molecules called secondary metabolites. Secondary metabolites are not necessary for a cell (organism) to measure; however plays crucial role in ensuring the continuing existence of organism because it interferes within the interaction of cell with its surroundings. They shield plants against stresses, each organic phenomenon (nematodes, insects, fungi or animal grazing) and abiotic (moisture and higher temperature, heavy metals presence or injury). Secondary metabolites are used particularly as chemicals like medicines, fragrances, flavours, dyes and insecticides by human attributable to their nice measures. Secondary metabolites are characterised into three categories: Terpenes, Phenolic Compounds and Alkaloids and Sulfur compounds. Among these, Polyphenols are naturally occurring compounds found largely in the beverages, fruits, vegetables and cereals. Polyphenols are involved in defense against aggression by pathogens or ultraviolet radiation. Phenolic Compounds are sub- categorised into Anthocyanins, No flavonoids, Tannins and Flavonoids. Flavonoids are the most abundant and mostly studied group of Polyphenols.

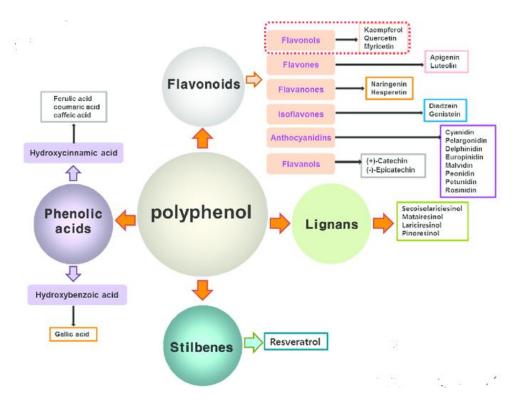


Figure 1: Classification of Polyphenols [1]

Flavonoids possess biological activities including antiallergenic, anti-inflammatory, antiviral and vasodilating actions. Flavonoids mostly found in vegetables, fruits, and certain beverages and largely derived from onion, have versatile beneficial antioxidant effects. A large number of varieties of flavonoids have been identified, and advantage of their potential beneficial effect on human health such as properties like antiplatelet, antiviral, anti-inflammatory, anti-allergic, antitumor, antioxidant, and treatment of neurodegenerative disorders makes flavonoid study of particular interest. Flavonoids are arranged into six classes as per the substance structure into flavonones, flavonols, flavonols, isoflavones, flavones, and anthocyanidins.

Quercetin (3,3',4',5,7- pentahydroxy-flavone) [C₁₅H₁₀O₇], is one in all the foremost long flavonol found in fruits and vegetables. It possesses sturdy health edges, radical scavenging property sensitive to environmental changes like that in hydrogen ion concentration (pH), solvent polarity, use of micellar media, etc. The utilization of such flavonoids has been restricted, thanks to their instability and poor water solubility, low availableness and poor porosity under conditions encountered throughout food/pharmaceuticals merchandise processing (temperature, pH, light), within the gut (enzymes, pH, presence of alternative nutrients) or throughout storage (light, oxygen). These factors limit the benefits, the edges and potential health advantages of these compounds in useful food or pharmaceutical merchandise. These limitations can be overcome by use of surface-active agent nano-cavities, identified to resist degradation of pharmacologically active molecules and enhance bioavailability.

Surfactants are the surface dynamic operators which diminishes the surface strain of fluids by bringing down the interfacial pressure between two fluids. Surfactants are flexible synthetic mixes which are amphiphilic in nature comprising of hydrophilic head (anionic, cationic, non ionic and zwitterionic) and a hydrophobic tail. Indeed, even in little sum, these surfactants have capacity to modify the surface or interfacial free energies to a checked degree because of their property of adsorbing onto the interfaces or surfaces of the framework. Thus, surfactants are widely preferred in industrial applications such as dispersing, emulsifying, cleaning, washing, medicines, etc. Interaction of Quercetin flavonol with cationic surfactant has proven to be electrochemically stable.

Cetyltrimethyl ammonium bromide $[(C_{16}H_{33})N(CH_3)_3Br]$, is a quaternary ammonium cationic surfactant. Its use is preferred in topical antiseptic cetrimide. It has been proved to be an effective antiseptic agent against microorganisms bacteria and fungi. It is also preferred as extraction buffer in DNA isolation.

Since surfactant blends have characteristic presence in various nourishment details/organic frameworks, because of their proficient solubilization, suspension, scattering, and transportation capacities, concentrating the communication of dietary flavonoid, Quercetin, with the blended micelles of cationic surfactants and subsequently its resulting effect on its general properties merit consideration. The reports with respect to the impact of double and tertiary blended micelles on the general movement of bioactive particles are rare and thus one of the principle destinations of the present examination.

The information of molecular mechanism of drug-membrane interaction is not solely of theoretical importance, however additionally of potential sensible implications [2]. For diagnosing, treatment, cure and prevention of a disease, drug molecules are preferred as these alter the physiological system of the body. Drug molecules are characterized by the presence of various useful functional groups such as polar (hydrophillic) and non-polar (hydrophobic) groups that are responsible for their therapeutic properties. So, a scientific information of the solution behavior of drug/molecules excipients is of great significance in understanding their physiological action [3]. Chemically, the drug action is represented as:

 $Drug (D) + Receptor (R) \iff Drug Receptor Complex (DR) \implies Response$

The interaction between drug and body are conveniently divided into two classes [4]:

- (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/molecule excipients and functionally important molecules in the living organism. The term excipient means to receive, to assemble and to take out which signifies one among the properties of an excipient to confirm that a medicative product has weight, consistency and volume necessary for proper administration of the active principle.

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 numerous physicochemical properties chiefly decided by various interactions e.g. ionic, hydrogen bonding, charge transfer, covalent or hydrophobic interaction, etc. Transport property measurements are a powerful tool to study the behavior of assorted solutes/drugs in solutions.

Thermodynamic parameters as Change in Enthalpy (ΔH°_{m}), Entropy (ΔS°_{m}) and Gibbs free energy (ΔG°_{m}) of micellization and Thermoacoustic parameters as ultrasonic velocity, viscosity, density and pressure plays a vital role in Absorption, Digestion, Metabolism and Excretion(ADME) pathway inside human body by entering as excipient. Rising resistance has demanded the study of these parameters while forming a formulation. So, an optimal concentration of flavonoid on interaction with surfactant will result into formation of useful topical formulations.

In this project, various parameters have been studied and techniques have been used to study the effect of intermolecular interactions of Quercetin (flavonoid) and CTAB (surfactant) in aqueous medium.

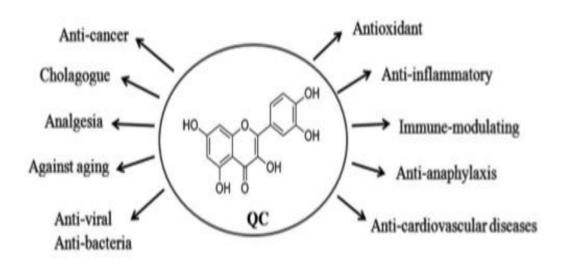
1.2 Background/Review of Literature:

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

Quercetin, a plant-derived aglycone form of flavonoid glycosides, is useful against variety of diseases and conjointly used as nutritional supplement. Some of the beneficial effects include anti-infective, immunomodulatory, antihypertensive, gastroprotective effects, anti-diabetic, anti-viral, anti-allergy, anti-ulcer, antitumor, anti-inflammatory activity, anticancer and cardiovascular protection [5].

In B16 melanoma cells of mouse, Quercetin acts as melanogenesis inhibitor, a potent tyrosinase inhibitor, and an anticancer and antioxidant agent [6–10]. Following dose dependant manner, in B16 melanoma cells melanin production is being inhibited by Quercetin [11]. However in human melanoma cells, it has the opposite effect as a melanogenesis accelerator [6,12-17]. In its structure, Quercetin consists of heterocyclic pyrone ring, connected to phenolic moieties on both sides. It exists in the form of rutin

(quercetin-3-rutinoside), a glycoside containing a disaccharide covalently attached to the quercetin unit Figure 2 [15,17-19].



As a therapeutic agent, Quercetin potential health benefits can be stated as:

Figure 2: Health benefits of Quercetin [20]

Inflammation, a self-protection biological response generated when parts of human body are exposed to irritating or harmful stimuli. Its aim is to evacuate pathogens, any harmful stimuli or damaged cells and to initiate healing process. The inflammation process is the body's reaction trying to heal itself. A standout amongst the most amazing properties of Flavonoid Quercetin, is its capacity to adjust irritation and modulate inflammation. Quercetin inhibits enzymes that serves as the cause of inflammation like lipooxygenase and cyclooxygenase(COX) decreasing the leukotrienes and prostaglandins which are inflammatory mediators [21.22].

In most countries, Morbidity and Mortality rate is increasing at rapid state and the main cause of this increase is Cardiovascular diseases [23]. Greek Cardiologist conducted a study on thirty men who had coronary heart disease(CHD), It has been reported that Red Grape polyphenol extract consumption rich in Quercetin caused an increase in flow-mediated dilation of arteries, indicating improved endothelial health [24].

Quercetin improves the health of the endothelium and inhibits platelet aggregation. It reduces the risk of mortality caused by low-density lipoprotein(LDL). It also protects against Coronary Heart disease. Quercetin exhibit important vasorelaxtant properties on isolated arteries which prevents the development of cardiac hypertrophy and also helps to lower blood pressure [25]. Studies reveal that people who intake high amount of Flavonoid containing food supplements have lower cholesterol. In one of the study, it has been found that intake of Quercetin and alcohol-free red wine extract inhibits LDL oxidation [26].

Epidemiological study showed that the diet with more fruits and vegetables provides protection against cancer. Quercetin has anticancer properties which include growth factor suppression, antiproliferative and antioxidant [26]. Quercetin has potent anticarcinogenic properties. It also contributes as apoptosis inductor whereby it inhibits the spread of malignant cells and also decreases the tumor growth in brain, colon, liver, and other tissues [27-28].

Quercetin is known to exhibit antibacterial effects against almost all strains of bacteria, particularly affecting respiratory, urinary, gastrointestinal and dermal system. Their anti-replicative and anti-infective ability contributes to the antiviral characteristics. Viruses which commonly respond to flavonoids are Japanese encephalitis virus, respiratory syncytial virus, herpex simplex virus and adenovirus [29-31].

Quercetin exerts anti-allergy effects, act as a natural antihistamine, prevents the mast cells and other allergic substances from releasing histamine. Quercetin advantages have tremendous implications for treatment and prevention of asthama and bronchitis due to its ability to prevent allergic effects. The cell membrane of mast cells acts as immune gateway to the brain, the environment and emotional stress [32].

Quercetin when used in combination with fish oil showed features of neuroprotection in rat brain. It also showed beneficial effects against neurodegenerative disease [33-34].

In Pharmacokinetics, Ferry et al. studied the dose levels from $60-2000 \text{ mg/m}^2$ of intravenous injection of Quercetin on cancer patients. It has been determined that the safety dose of Quercetin is 945 mg/m². In toxic dose, quercetin caused hypertension, nephrotoxicity, emesis and reduction in serum potassium [35].

Novel delivery strategies like with liposomes/phospholipid complexes and formulations, inclusion complexes QC nanocrystals were used. Novel delivery strategy system faces problems as Lower drug loading and encapsulation efficiency, incomplete degradation of carrier, accumulation in organs and drug targetting. The inclusion of Cyclodextrin created risk of Nephrotoxicity [36].

The Quercetin antioxidant activity is observed to be more in the cationic surfactant than in anionic and non-ionic surfactant systems. Interaction of Quercitin with cationic surfactant is electrochemically stable and radical scavenging was best observed in cationic surfactant [20]

Presence of Decamethoxin (antiseptic drug) in cation solution favours tautomeric transition of enol to keto form of QC which provides greater Bond energy [37]. QC solubility increases with increasing temperature. Solubility of Quercetin is observed more in solution containing water and Ethanol as compared to that of solubility in solution containing water and methanol [38].

Cationic surfactant CTAB ($C_{19}H_{42}BrN$) having molecular weight 364.45g/mol -Cetyltrimethyl ammonium Bromide. It is a Quaternary ammonium surfactant. CMC of CTAB is 1mM at 25°C. Its structure is as follows:

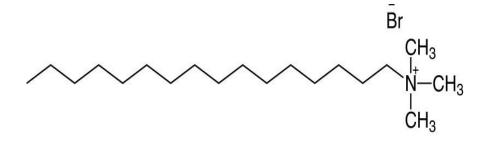


Figure 3: Structure of cationic surfactant CTAB

Adsorption of CTAB decreases with increasing temperature signifying exothermic natured process [39]. Absorption rate of CTAB is high on low doses. Strong alcohol-aqueous surfactant interactions results in decrease in magnitude of CMC on addition of alcohol [40]. Conductivity of CTAB increases with both increasing temperature and salt concentration(NaBr) [41].

The role, safety and importance of pharmaceutical excipients with respect to Active Pharmaceutical Ingredients have been examined. Most part of the medicine as far as its weight is concerned is constituted by excipients which guarantee the stability, dosage, and bioavailability of the active principle. The review of principle classes of excipients and its side effects have been examined in this review article [42]. The drug excipient interactions stated that although excipient be pharmacologically inert, it can intiate, participate or propagate in physical or chemical interactions with drug compounds, which may compromise the medicinal effectiveness [43].

The surfactant applications have been reviewed stating important role of surfactant in drug deliveries. The surfactants or pharmaceutically acceptable co-solvents have been employed to formulate compounds sparingly soluble in water. The surfactant system increases the solubility by guiding the mechanism to form micelles [44].

1.3 **Objectives:**

To determine the following parameters of Quercetin with cationic surfactant CTAB:

- Specific Conductance
- Viscosity
- Velocity
- Density

Utilizing these studies to calculate various thermodyamic and thermoacoustic parameters i.e.

- Change in enthalpy (ΔH°_{m}) , entropy (ΔS°_{m}) and Gibbs free energy (ΔG°_{m})
- Apparent Molar Volume (ϕ_v)
- Apparent Adiabatic Compressibility (ϕ_k)

CHAPTER-02

MATERIALS AND METHODOLOGY

2.1 Materials/Equipment Used

2.1.1 Temperature Control and Thermostat:

All the measurements has been carried out in an automatic digital temperature controller high precision water thermostat (HARCO) having temperature control of accuracy $\pm 0.05^{\circ}$ C.

2.1.2 Conductivity Meter:

It measures the amount of electrical current or conductance in a solution. It is useful in determining the overall health of a natural water body. It is based on the principle of measurement of ions by applying potential across the plates immersed in solution.

Electrical Conductivity is denoted by symbol sigma (σ)

Its SI unit is **Siemens per metre** $(S \cdot m^{-1})$

Electric Conductivity depends on :

- Concentration of ion
- Temperature of the solution
- Specific nature of the ions

2.1.3 Viscometer:

An ubbelohde type viscometer or suspended-level viscometer is a measuring instrument which uses a capillary based method of measuring viscosity. The instrument is best suited for higher viscosity cellulosic polymer solutions.

The value obtained are independent of the total volume.

Viscosity is denoted by symbol eta $(\dot{\eta})$ and its SI unit is centipoises(cp)

2.1.4 Ultrasonic Velocity Meter:

Ultrasonic Velocity meter measures the velocity of fluid with ultrasound to calculate volume flow. It measures the difference between the transit time of ultrasonic pulses propagating with and against the flow direction.

Velocity is denoted by μ and its SI unit is m/s

2.2 Methodology

2.2.1 Conductance Measurement :

- Different solutions of Quercetin of different concentrations 1mM, 2mM and 3mM has been prepared with different solutions as in distilled water, 30% Ethanol, 70% Ethanol and 100% Ethanol.
- Surfactant concentration has been varied by successive addition of small installments of surfactant stock solution using pipette.
- The solutions conductivity has been measured at different temperatures as 20 °C, 25 °C, 30 °C, 35 °C and 40 °C.
- The cmc values of all the solutions have been determined from the plot of Conc. v/s Conductivity measured by conductivity meter.

2.2.2 Thermodynamic parameters:

The X_{CMC} data has been used to determine the thermodynamic parameters. The values of standard enthalpy change (ΔH°_{m}), standard entropy change (ΔS°_{m}) and standard Gibbs free energy change (ΔG°_{m}) has been calculated using following equations:

$$\Delta H_{m}^{o} = -RT^{2} (2 - \alpha) [d (ln X_{CMC}) / dT]$$
 (i)

$$\Delta G_{m}^{o} = (2 - \alpha) \operatorname{RT} (\ln X_{CMC})$$
(ii)

$$\Delta S^{o}_{m} = (\Delta H^{o}_{m} - \Delta G^{o}_{m}) / T$$
 (iii)

The d(ln X_{CMC})/dT denoted the slope of the straight line obtained by plotting ln X_{CMC} against temperature. The degree of ion dissociation (α), has been calculated from the relation, $\alpha = S_2/S_1$, where S_1 and S_2 are the slopes in the pre micellar and post micellar region.

2.2.3 Density and ultrasonic sound velocity measurements

The density (ρ) has been manually calculated with the help of specific gravity bottle and calibrated weighing balance. The ultrasonic sound velocity (μ) values has been calculated from Digital Ultrasonic Pulse-Echo Velocity meter for Liquids and Solids (VCT-70A), supplied by Vi Microsystems Pvt. Ltd., Chennai. The density and ultrasonic sound velocity values have been calculated for various concentrations of ethanol and surfactant at three different concentrations of Quercetin (1-3 mM).

2.2.4 Relative viscosity measurements:

The viscosity (η) measurements have been carried out in a calibrated jacketed ubbelhode viscometer. The desired temperature has been achieved with the help of water thermostat having a digital temperature controller, purchased from Harsh & Co., Ambala. From the obtained values, relative viscosities has been calculated by using the equation:

$$\eta_r = \eta/\eta_o = (t \times \rho)/(t_o \times \rho_o)$$
(iv)

Here η , t and ρ are the viscosity, flow time and density of solution and η_o , t_o and ρ_o of solvents, respectively.

2.2.5 Apparent molar volume (ϕ_v) and apparent adiabatic compressibility (ϕ_k)

Density (ρ) and ultrasonic sound velocity (μ) values have been used to measure apparent molar volume and apparent adiabatic compressibility using the following relations:

$$\phi_k = \frac{1000(\beta - \beta_0)}{c.\rho_0} + \beta.\phi_v \tag{v}$$

$$\phi_{\nu} = \frac{1000}{c} \left\{ \frac{\rho_0 - \rho}{\rho_0} \right\} + \frac{M}{\rho_0} \tag{vi}$$

where, c is the concentration of surfactant, ρ is the density of solution, ρ_0 is the density of solvent system, M is the molecular weight of surfactant, β and βo are the adiabatic compressibility of the solution and solvent respectively, calculated from the relation $\beta = 1/\rho\mu^2$.

CHAPTER-03 RESULTS AND DISCUSSION

3.1 Results and Discussion :

3.1.1 Specific conductance

The values of CMC has been obtained by plotting the graph between specific conductance and surfactant concentration (Table 1). According to the literature, CMC of CTAB in pure water is 1mM [25°C]. In all the solutions, it has been found that the CMC values increases with increase in temperature.

Table 1. CMC data obtained by interaction of Quercetin (1-3 mM) with different concentrations of CTAB at different temperatures (20-40 °C)

	CMC	(0% E	tOH)	CMC	(30% I	EtOH)	CMC (70% E	tOH)	CMC (100% EtOH)			
Temp (°C)	1mM	2mM	3mM	1mM	2mM	3mM	1mM	2mM	3mM	1mM	2mM	3mM	
20	0.9	1.4	1.12	1.15	1.05	1	1.1	1.12	1.05	1.15	1.17	1.2	
25	1	1.5	1.14	0.95	1.1	1.05	1.15	1.15	1.1	1.25	1.3	1.25	
30	1.07	1.52	1.23	0.93	1.17	1.15	1.2	1.28	1.15	1.27	1.32	1.3	
35	1.1	1.54	1.3	0.9	1.25	1.3	1.25	1.22	1.2	1.29	1.38	1.32	
40	1.5	1.6	135	0.85	1.3	1.25	1.28	1.25	1.25	1.32	1.4	1.37	

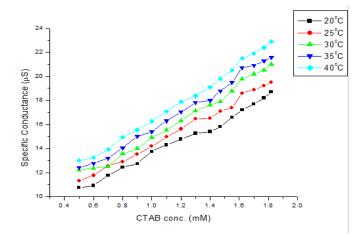


Figure 4: Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 1mM Quercetin.

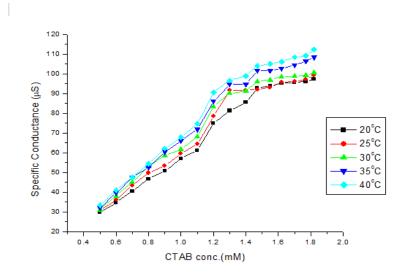


Figure 5: Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 2mM Quercetin.

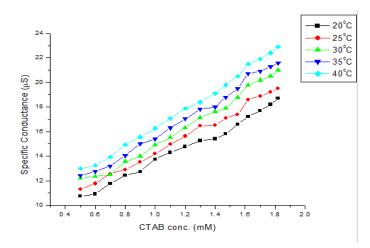


Figure 6: Variation of Specific Conductance (κ) with concentration of CTAB at different temperature in 3mM Quercetin.

3.1.2 Thermodynamic parameters:

The values of thermodynamic parameters i.e. standard enthalpy change (ΔH^{o}_{m}) , standard entropy change (ΔS^{o}_{m}) and standard Gibbs free energy change (ΔG^{o}_{m}) for different concentrations of Quercetin (1-3 mM) in pure water are given in Table 2. Table 3, 4 and 5 represents the thermodynamic parameters for different concentrations of Quercetin (1-3 mM) in ethanol.

QC. Conc.	T(°C)	СМС	X _{CMC}	ΔH^{o}_{m}	ΔG ^o m	ΔS^{o}_{m}
	20	0.0009	1.62011E-05	0.711678	-1.16614	0.093891
	25	0.001	1.80012E-05	1.111998	-1.43578	0.101911
1mM	30	0.00107	1.92612E-05	1.601276	-1.70606	0.110244
	35	0.0011	1.97909E-05	2.179515	-1.98235	0.118911
	40	0.0015	2.70015E-05	2.846714	-2.1624	0.125228
2	20	0.00147	0.423631124	0.678422	-1.08456	0.088149
	25	0.0015	0.428571429	1.060035	-1.3515	0.096461
2mM	30	0.00152	0.431818182	1.52645	-1.6185	0.104832
	35	0.00154	0.435028249	2.077669	-1.88444	0.113209
	40	0.0016	0.44444444	2.71369	-2.14094	0.121366
	20	0.00112	2.01605E-05	0.701702	-1.12978	0.091574
	25	0.00114	2.05205E-05	1.096409	-1.40854	0.100198
3mM	30	0.00123	2.21405E-05	1.578829	-1.6713	0.108338
	35	0.0013	2.34005E-05	2.148961	-1.93374	0.116649
	40	0.00135	2.43005E-05	2.806806	-2.19744	0.125106

Table 2: Thermodynamic parameters for different concentrations of Quercetin (1-3 mM) inpure water at different temperatures (20-40 $^{\circ}$ C)

QC. Conc.	T(°C)	СМС	X _{CMC}	ΔH^{o}_{m}	ΔG ^o m	ΔS ^o m
	20	0.00115	2.06905E-05	0.731632	-1.12538	0.092851
	25	0.00095	1.70922E-05	1.143175	-1.44644	0.103585
1mM	30	0.00093	1.67324E-05	1.646172	-1.74103	0.112907
	35	0.00090	1.61926E-05	2.240623	-2.04075	0.122325
	40	0.00085	1.5293E-05	2.926528	-2.35129	0.131945
	20	0.00105	1.88913E-05	0.705027	-1.14051	0.092277
	25	0.00110	1.97909E-05	1.101605	-1.41597	0.100703
1mM 2mM 3mM	30	0.00117	2.10503E-05	1.586311	-1.68377	0.109003
	35	0.00125	2.24896E-05	2.159146	-1.94516	0.117266
	40	0.00130	2.33892E-05	2.820109	-2.20999	0.125753
	20	0.001	1.79918E-05	0.708353	-1.14862	0.092849
	25	0.00105	1.88913E-05	1.106801	-1.42564	0.101297
3mM	30	0.00115	2.06905E-05	1.593794	-1.68807	0.109396
	35	0.0012	2.159E-05	2.16933	-1.95703	0.117896
	40	0.00125	2.24896E-05	2.833411	-2.22303	0.126411

Table 3: Thermodynamic parameters for different concentrations of Quercetin (1-3 mM) in30% v/v ethanol at different temperatures (20-40 °C)

QC. Conc.	T(°C)	СМС	X _{CMC}	ΔH^{o}_{m}	ΔG^{o}_{m}	ΔS ^o m
	20	0.0011	0.035369775	0.705027	-1.13277	0.09189
	25	0.00115	0.036918138	1.101605	-1.40673	0.100333
1mM	30	0.0012	0.038461538	1.586311	-1.67746	0.108792
	35	0.00125	0.04	2.159146	-1.94516	0.117266
	40	0.00128	0.040920716	2.820109	-2.21515	0.125881
	20	0.00112	2.01507E-05	0.69505	-1.12978	0.091241
	25	0.00115	2.06905E-05	1.086016	-1.40673	0.09971
2mM	30	0.0018	3.23847E-05	1.563863	-1.57633	0.104679
	35	0.00122	2.19499E-05	2.128592	-1.95222	0.116595
	40	0.00125	2.24896E-05	2.780202	-2.22303	0.125081
	20	0.00105	1.88913E-05	0.708353	-1.14051	0.092443
	25	0.0011	1.97909E-05	1.106801	-1.41597	0.100911
3mM	30	0.00115	2.06905E-05	1.593794	-1.68807	0.109396
	35	0.0012	2.159E-05	2.16933	-1.95703	0.117896
	40	0.00125	2.24896E-05	2.833411	-2.22303	0.126411

Table 4: Thermodynamic parameters for different concentrations of Quercetin (1-3 mM) in70% v/v ethanol at different temperatures (20-40 $^{\circ}$ C)

QC. Conc.	T(°C)	СМС	X _{CMC}	$\Delta H^{o}{}_{m}$	ΔG ^o m	ΔS^{o}_{m}
	20	0.00115	2.06905E-05	0.698376	-1.12538	0.091188
	25	0.00125	2.24896E-05	1.091213	-1.3894	0.099224
1mM	30	0.00127	2.28494E-05	1.571346	-1.66332	0.107822
	35	0.00129	2.32092E-05	2.138777	-1.93599	0.116422
	40	0.00132	2.3749E-05	2.793504	-2.20491	0.12496
	20	0.00117	2.10503E-05	0.69505	-1.12251	0.090878
	25	0.0013	2.33892E-05	1.086016	-1.38124	0.09869
	30	0.00132	2.3749E-05	1.563863	-1.65369	0.107252
2mM	35	0.00138	2.48285E-05	2.128592	-1.91636	0.11557
	40	0.0014	2.51883E-05	2.780202	-2.18535	0.124139
	20	0.0012	0.038461538	0.69505	-1.11831	0.090668
	25	0.00125	0.04	1.086016	-1.3894	0.099017
3mM	30	0.0013	0.041533546	1.563863	-1.65749	0.107379
	35	0.00132	0.042145594	2.128592	-1.9293	0.11594
	40	0.00137	0.043672298	2.780202	-2.19255	0.124319

Table 5: Thermodynamic parameters for different concentrations of Quercetin (1-3 mM) in100% v/v ethanol at different temperatures (20-40 °C)

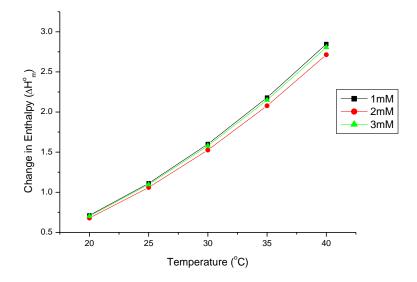


Figure 7: Graphical representation of Change in Enthalpy (ΔH°_{m}) vs. Temperature for different concentrations of QC (1-3mM) in aqueous solution.

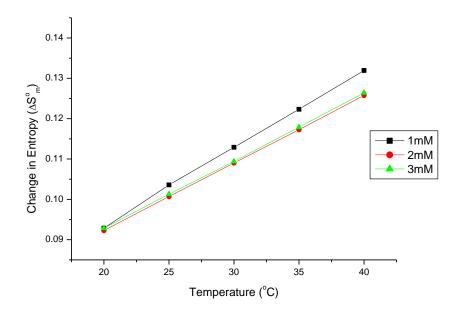


Figure 8: Graphical representation of Change in Entropy (ΔS°_{m}) vs. Temperature for different concentrations of QC (1-3mM) in 30% v/v Ethanol solution

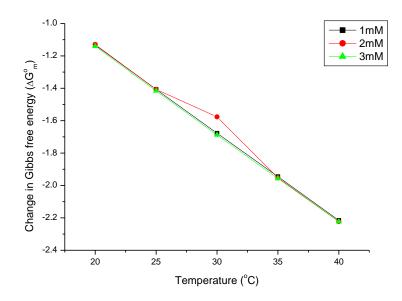


Figure 9: Graphical representation of Change in Gibbs free energy (ΔG°_{m}) vs. Temperature for different concentrations of QC (1-3mM) in 70% v/v Ethanol solution.

The data clearly shows that the values of ΔG^{o}_{m} in water and hydro-ethanolic solutions has been found to be negative for all concentrations and temperatures. On the other hand, the values of ΔH^{o}_{m} and ΔS^{o}_{m} has been found to be positive. The value of ΔS^{o}_{m} indicates that micellization in these studied systems is entropically controlled. The studies also suggest that the interactions between Quercetin and CTAB are endothermic in nature. The activity of Quercetin has been best observed at 40 °C for all concentrations of CTAB and hydro-ethanolic solutions.

3.1.3 Density and ultrasonic sound velocity measurements:

The density (ρ) and ultrasonic sound velocity (μ) has been measured for CTAB in presence of Quercetin (1-3 mM) at five different temperatures and four different hydro-ethanolic solutions. It has been found that the density and ultrasonic sound velocity are completely concentration and temperature dependent in all solution systems. The results of density and ultrasonic sound velocity are displayed in Table 6 and 7 respectively.

3.1.4 Relative viscosity measurements

The relative viscosity measurements of CTAB and Quercetin in pure ethanol, ethanol rich, water rich and pure water compositions have been conducted at five different temperatures. The viscosity values have been found to increase with increase in temperature at all temperatures and ethanolic concentrations. However, a decrease in values has been observed near the CMC values confirming that the micellization has been occurred. The values of relative viscosities are presented in Table 8.

3.1.5 Apparent molar volume (ϕ_v) and apparent adiabatic compressibility (ϕ_k)

Density (ρ) and ultrasonic sound velocity (μ) values have been used to measure apparent molar volume and apparent adiabatic compressibility. These parameters helped us in determining different kinds of interactions furnished by solute in the solution so that the structural consequences arising from solute-solvent interactions can be studied. The values obtained for apparent molar volume and apparent molar compressibility are represented in Tables 9 and 10 respectively. **Table 6:** Density, ρ (g cm⁻³) obtained by interaction of Quercetin (1-3 mM) with different concentrations of CTAB (0.5-1.77 mM) and ethanol at

five different temperatures.

		40 °C	0.7821	0.7904	0.7894	0.7898	0.7896	0.7895	0.7904	0.7908		0.7874	0.7886	0.7874	0.7874	0.7876	0.7878	0.7881	0.7886		0.7851	0.7862	0.7852	0.7853	0.7874	0.7856	0.7864	0.7864															
H		35 °C	0.7812	0.7924	0.7965	0.7874	0.7884	0.7914	0.7946	0.7974		0.7812	0.7902	0.7943	0.7856	0.7861	0.7896	0.7934	0.7956		0.7782	0.7881	0.7924	0.7836	0.7845	0.7876	0.7912	0.7953															
100% v/v EtOH		30 °C	0.7891	0.7942	0.7984	0.7905	0.7916	0.7945	0.7972	0.8004		0.7941	0.7925	0.7964	0.7834	0.7896	0.7924	0.7952	0.7963		0.7856	0.7901	0.7942	0.7862	0.7874	0.7904	0.7894	0.7963															
100% 1		25 °C	0.8590	0.8612	0.8604	0.8584	0.8601	0.8604	0.8605	0.8604		0.7915	0.7926	0.7954	0.7976	0.7945	0.7998	0.8014	0.8002		0.7890	0.7901	0.7936	0.7952	0.7924	0.7976	0.7982	0.798.5															
		20 °C	0.8642		0.8605	0.8647	0.8651	0.8654	0.8664	0.8885		0.8441	0.8632	0.8405	0.8445	0.8452	0.8457	0.8465	0.8840		0.8270	0.8635	0.8204	0.8245	0.8247	0.8256	0.8304	0.8642															
		40 °C	0.7824 (0.7865 (0.8056 (0.8074 (0.8154 (0.8172 (0.8542 (0.8782 (0.8784 (0.8793 (0.8795 (0.8797 (0.8786 (\vdash	0.8790 (0.8782 (0.8795 (90	0.8777 (0.8779 (0.8795 (0.8784 (0.8796 (
		ç	0.8651 0	0.8702 0	0.8691 (8686 (0.8689 (0.8672 (0.8665 (0.8668 (0.8641 (0.8651 (n	0.8705 0	8706 0	0.8691 (0.8682 0	0.8682 0		0.8661 0	0.8674 0	0.8738 0	8724 0	8729 (0.8719 0	0.8704 0	0.8708													
EtOH		°C 35	_	\vdash		•	8732 0.5		-	\vdash		⊢	8784 0.5	62 0.87		0	⊢	\vdash			E.	8804 0.5	⊢	8824 0.5	8735 0.8	⊢		5															
70% v/v EtOH		8	2 0.862	•	6 0.8680	2 0.8901	•	•	5 0.8805	7 0.8725		1 0.8624	0	2 0.8662	4 0.882	2 0.8712	5 0.8704	4 0.8764	5 0.8672		0 0.8831	•	5 0.8680	•	0	9 0.8725	1 0.8806	6 0.871															
		25 °C	0.8802	0.8804	0.8816	0.8732	0.8885	0.8890	0.8895	0.8897		0.8781	0.8790	0.8792	0.8804	0.8762	0.8785	0.8804	0.8815		0.8810	0.8824	0.8835	0.8790	0.8836	0.8839	0.885	0.8836															
	(JmM)	20 °C	0.8832	0.8837	0.8842	0.8849	0.9012	0.9021	0.9024	0.9102	(Wm	0.8820	0.8835	0.8605	0.8825	0.8836	0.8845	0.8847	0.8849	mM)	0.8801	0.8884	0.8584	0.8802	0.8814	0.8824	0.8828	0.8829															
	Duercetin (1m	40 °C	0:630	01610	0.920	0.940	0.924	0.924	0.945	0.930	Quercetin (2mM)	0.9120	0.9210	0.9340	0.9142	0.9420	0.9092	0.9301	0.9230	uercetin (3mM)	0.9139	17120	0.9179	0.9223	0.9231	0.9271	0.9293	0.9311															
H	ō	35 °C	0.927	0.932	0.942	0.975	0.986	0.915	0.935	0.957	ō	0.9452	0.9453	0.9422	0.9475	0.9496	0.9363	0.9432	1.0542	ō	0.9912	0.9919	0.9920	0966-0	0.9872	1.010	0.9792	0.9735															
30% v/v EtOH		30 °C	0.930	0.921	0.907	016.0	906-0	0.902	0.903	0.913		0.932	0.933	0.935	156.0	0.937	0.948	0.948	0.943		0.9972	0.9940	0.9894	0.9742	0.9762	0.9736	0.9719	0.9765															
30		25 °C	0.941	0.950	0.932	0.934	0.942	0.941	0.940	0.932		0.953	0.959	0.965 0.966 0.971	1/2/0	172.0	0.975	275.0		09860	0666-0		0.9862		0.9882	0.9925	0.9836																
		20 °C	0.954	0.942	0.912	0.923	0.974	0.942	0.935	0.915																	0.979	186.0	0.989	066-0	0.989	0.992	166'0	0.992		1066-0	0.9920	0.9927	0.9929	0.9935	5965.0	0.9939	0.9949
		40 °C	966'0	16610	0.993	0.994	0.984	0.981	0.988	0.984		166'0	0.993	0.987	0.984	0.987	566.0	0.995	966'0		0.993	0.985	0.990	0.990	0.990	0.989	0.987	0.986															
_		35°C	866.0	0.993	566.0	966'0	986'0	0.983	066-0	0.986		0.994	866.0	966-0	0.986	586.0	066'0	0.985	0.986		0.994	0.980	16610	0.992	16610	06610	0.987	0.986															
0% v/v EtOH		30 °C	1.003	1.003	1.003	666-0	0.9929	0.9927	0.9937	0.9933		966'0	966-0	966-0	0.987	0.987	0.992	0.988	0.988		966-0	966-0	16610	066-0	066-0	166'0	0.990	0.987															
60		25 °C	1.009	1.019	1.013	1.011	1.015	1.009	1.015	1.013		666-0	566.0	1.003	0.989	0.989	066-0	066-0	166'0			660	0.993	0.992	0.992	0.993	0.992	066-0															
		20 °C	966'0	0.997	966.0	666 0	1.001	1.011	0.998	0.998		086.0	0.989	0.993	0.9878	0.9872	0.989	0.990	06610		0.989	0.987	0.988	16610	0.993	0.990	16610	566.0															
CTAB [mol kg ⁴]			5.0	0.7	60	11	ธ	1.47	1.62	1.77		50	0.7	60	11	ព	1.47	1.62	1.77		50	0.7	60	=	ព	1.47	1.62	177															

Table 7: Ultrasonic sound velocity, μ (m s⁻¹) obtained by interaction of Quercetin (1-3 mM) with different concentrations of CTAB

(0.5-1.77 mM) and ethanol at five different temperatures

		40 °C	1114.7	1117.8	1121.1	1123.7	1123.8	1123.8	1124.1	1123.1		1112.74	1115.83	1115.83	1111.12	1113.74	1113.88	1114.12	1113.11		1102.74	1105.83	1105.83	1101.12	1103.74	1103.88	1104.12	1102 11			
H		35 °C	1134.3	1135.7	1140.3	1141.5	1142.7	1143.7	1141.5	1140.7		1124.34	1125.70	1130.31	1131.52	1132.73	1133.71	1131.52	1130.71		1114.34	1115.70	1120.31	1121.52	1122.73	1123.71	1121.52	1100.011			
100% v/r EtOH		30 °C	1133.2	1133.7	1134.1	1133.0	1131.1	1131.1	1134.0	1133.0		1123.2	1123.6	1124.1		1113.68	1114.10	1113.07	1111.12	1113.04	1114.01	1119 00									
		25 °C	1217.4	1224.9	1228.7	1227.1	1230.4	1233.1	1235.4	1237.4		1132.71	1134.70	1136.30	1137.50	1136.70	1138.90	1137.70	1137.92		1122.71	1124.70	1126.30	1127.50	1126.70	1128.90	1127.70	1107 00			
		20 °C	1198.79	1214.41	1221.1	1223.4	1227.1	1229.5	1233.1	1234.5		1188.79	1214.41	1211.91	1188.17	1187.36	1184.17	1181.71	1186.41		1178.79	1204.41	1201.91	1178.77	1177.36	1174.17	1171.71	11 2011			
HOJ A/A 960L		40 °C	1359.53	1361.82	1364.70	1362.67	1363.55	1372.35	1368.74	1355.07		1359.53	1361.82	1364.70	1362.67	1363.55	1372.35	1368.74	1369.32		1349.53	1351.82	1354.70	1352.67	1353.55	1362.35	1358.74	1000.00			
		35 °C	1345.29	1347.12	1347.17	1342.04	1351.15	1334.17	1347.90	1342.87		1345.29	1347.12	1347.17	1342.64	1351.15	1334.17	1347.90	1342.87		1355.29	1357.12	1357.17	1352.64	1361.15	1344.17	1348.90	1969.00			
		30 °C	1328.69	1329.80	1332.80	1332.59	1333.70	1343.26	1343.88	1347.06		1328.69	1329.80	1332.80	1332.59	1333.70	1343.26	1343.88	1347.06		1338.69	1339.80	1342.80	1342.59	1343.70	1345.26	1343.88	1940 46			
		25 °C	1317.4	1324.9	1328.7	1327.1	1330.4	1333.1	1335.4	1337.4		1307.41	1314.91	1318.79	1317.15	1320.45	1323.17	1325.42	1327.41		1317.41	1324.91	1328.79	1327.15	1330.45	1333.17	1335.42	10001			
	N)	20 °C	1298.79	1314.41	1321.1	1323.4	1327.1	1329.5	1333.1	1334.5	(W	1288.79	1304.41	1311.19	1333.46	1327.10	1321.56	1323.14	1324.57	(W	1298.79	1314.41	1321.19	1343.46	1337.10	1331.56	1333.14	1004 60			
	Quercetin (1mM)	40 °C	1553.11	1544.01	1545.47	1545.47	1542.52	1544.47	1547.69	1549.18	Quercetin (2mM)	1503.06	1510.09	1512.92	1512.21	1515.75	1512.92	1516.04	1516.96	Quercetin (3mM)	1418.26	1430.15	1435.25	1437.24	1420.12	1412.35	1424.10	A1 0011			
н	ð	35 °C	1570.25	1567.99	1568.80	1570.25	1570.54	1572.54	1574.08	1573.33	ð	1531.36	1533.74	1538.12	1544.04	1543.32	1545.47	1549.18	1550.14	ð	1435.81	1445.70	1447.65	1449.09	1447.08	1444.70	1451.35	1464.46			
30% v/v EtOH		30 °C	1551.18	1551.90	1556.64	1561.90	1561.90	1562.24	1564.93	1570.25		1500.22	1512.92	1525.02	1532.28	1528.66	1521.46	1531.36	+	1431.18	1444.61	1445.90	1447.85	1443.32	1447.85	1450.45	1450 45				
9		25 °C	1560.40	1561.90	1564.97	1568 1571 1573 1573	1577.15		1444.61	1450.45	1451.10	1451.10	1453.71	æ	1453.71	1453.05		1430.18	1431.63	1437.72	1432.10		1447.20	1443.10	A1244						
		20 °C	1570.99	1570.25	1572.41	1573.31	1574.84	1575.61	1577.92	1579.46		1551.41	1552.80	1554.39	1558.14	1555.14	1557.30	1555.14	1556.17		1432.92	1435.63	1434.99	1445.26	1449.15	1455.02	1453.71	146.6 00			
		40 °C	1462.6	1460.28	+ $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$										1464.25	1462.92	1462.99	1455.67	1455.67	1456.33	1458.11	1459.10		1466.20	1467.10	1467.20	1460.10	1460.10	1461.08	1460.11	1464 10
н		35 °C	1440.10	1451.40	1450.45		1456.99	1468.24	1462.92	1462.92		1452.30	1452.30	1453.10	1455.30	1455.30	1456.10	1453.40	1453.40		1460.28	1461.60	1461.60	1462.26	1460.25	1460.94	1458.20	1466 67			
0% v/v EtOH		30 °C	1439.96	1426.61	1429.91	1436.26	1447.35	1448.20	1451.34	1453.30					1451.75	1451.75	1452.40	1453.05	1454.36	1454.36	1452.40	1452.40		1447.20	1448.21	1448.21	1449.30	1448.70	1452.10	1459.10	1440.10
		25 °C	1416.3	1418.61	1416.75	1422.98	1426.12	1424.87	1427.38	1431.81		1417.99	1418.61	1418.61	1418.40	1420.21	1424.31	1430.21	1434.20		1443.97	1446.45	1446.55	1446.65	1445.35	1451.10	1448.50	1447.05			
		20 °C	1426.75	1429.91	1428.01	1428.65	1428.65	1430.54	1429.91	1428.65		1436.26	1435.63	1436.20	1434.35	1434.35	1433.08	1432.45	1434.30		1417.99	1418.61	1418.61	1418.40	1420.21	1424.31	1430.21	10 1011			
CTAB [mol			0.5	0.7	0.9	1.1	13	1.47	1.62	1.77		0.5	0.7	0.9	1.1	13	1.47	1.62	1.77		0.5	0.7	0.9	1:1	13	1.47	1.62	5			

Table 8: Relative viscosity, n_h (centipoise) obtained by interaction of Quercetin (1-3 mM) with different concentrations of CTAB (0-1.77 mM) and ethanol at five different temperatures

	Γ	ų	28	2	31	8	21	8	36	<u>6</u>		2	Ŧ	8	4	11	20	22	2		5	5	10	4	=	8	2	2	
		\vdash		0.775	\vdash			0.790		0.789		0.724		0.718	0.744		\vdash	\vdash	0.755		0.69]	0.691	0.707	\vdash	0.71	0.695	0.720	0.720	
HO		35 °C	0.791	0.792	0.789	0.774	0.766	0.801	0.785	0.784		169:0	0.689	0.687	0.673	0.666	0.698	0.684	0.682		0.724	0.724	0.721	0.706	0.698	0.714	0.717	0.717	
100%6 v/v EtOH		30 °C	0.80	0.80	0.80	0.79	0.76	0.79	0.79	0.79		0.780	0.768	0.766	0.739	0.760	0.756	0.753	0.755		0.711	0.734	0.732	0.829	0.726	0.722	0.718	0.721	
10		25 °C	1.78	2.04	1.92	1.94	1.95	2.05	2.12	2.13		1.13	1.14	0.15	0.14	0.13	1.14	1.15	1.15		1.10	1.11	1.12	1.11	1.10	1.12	1.12	112	
		20 °C	2.07	2.02	1.98	2.01	2.09	2.15	2.17	2.24		1.68	1.62	159	1.62	1.69	2.78	1.77	1.78		1.61	1.58	1.52	155	1.62	1.68	171	1.79	
	1	40 °C	1.36	1.42	1.40	136	1.44	1.40	137	1.44		125	1.30	1.28	136	1.50	1.42	1.42	1.56		1.29	125	131	129	136	1.43	143	551	
_		35 °C	151	1.59	159	1.48	1.57	151	1.48	1.48		1.47	1.54	154	141	152	1.47	1.44	1.43		151	157	1.58	147	155	150	1.48	147	
70% v/v EtOH		30 °C	1.54	1.65	1.64	1.55	1.41	151	151	1.49		150	1.61	1.60	1.50	1.55	1.47	1.47	1.45		1.75	1.83	1.82	171	1.76	1.68	1.69	1.65	
60 <u>6</u>		25 °C	2.44	231	234	2.33	2.45	2.52	2.54	2.54		2.05	195	198195	1.98	195	2.06	2.17	2.19		2.10	1 99	2.10	199	2.11	221	222	224	
	R)	20 °C	2.47	237	239	2.40	2.54	2.60	2.62	2.66	NI)	2.09	1.56	198	20.6	2.13	220	221	2.23	M)	2.04	153	194	199	20.9	2.13	2.17	2.18	
	Quercetin (1mM	40 °C	135	1.28	121	1.19	1.28	122	1.24	125	Quercetin (2mM)	139	136	134	134	134	1.27	134	1.27	Quercetin (3mM)	0.712	0.715	0.717	0.724	0.743	0.755	0.746	0.727	
	8	35 °C	1.76	2	2.04	2.01	2	1.97	1.96	1.94	ð	1.66	151	150	1.44	141	139	1.41	1.59	Que O	0.655	0.668	0.973	0.662	0.666	0.674	0.677	0.660	
30% v/v EtOH		30 °C	1.59	1.63	1.66	1.69	171	1.74	1.80	1.84		2.06	2.08	2.18	2.11	2.18	1.89	2.05	2.05		0:750	0.752	0.747	0.756	0.731	0.731	0.761	0.768	
309		25 °C	0.788	0.809	0.805	0.803	0.799	0.813	0.821	0.809		2.65	2.83	3.07	3.01	2.72	2.78	2.90	2.69		0.788	0.826	0.848	0.852	0.872	0.876	0.845	0.833	
		20 °C	0.884	0.87	0.79	0.78	0.80	0.81	0.80	0.82		0.946	0.902	906-0	0.897	106-0	0.884	0.88	0.892		0.947	1.03	1.06	1.08	0.93	1670	0.922	0.927	
		40 °C	0.573	0.626	0.635	0.701	0.802	0.839	0.756	0.646		0.593	\vdash	0.631	0.634	0.668	0.810	0.677	0.681		0.566	0.582	0.582	0.612	0.582	0.720	0.582	0.582	
_		35 °C	0.573	0.625	0.635	0.700	0.802	0.840	0.757	0.646		0.667	0.662	0.680	0.626	0.706	0.664	0.700	0.674		0.723	0.685	0.664	0.667	0.673	0.680	0.678	0.689	
0%6 v/v EtOH		30 °C	0.872	0.815	0.831	0.849	0.851	0.835	0.827	0.819 0	1		0.719	0.707	0.719	0.746	0.706	0.741	0.706	0.714		0.895	0.958	0.892	106-0	0.904	0.890	0.890	0.890
60		25 °C	0.819	0.848	0.814	0.821	0.832	0.831	0.844	0.863		1.06	1.01	1.01	1.00	1.01	0.980	0.992	1.001		0.823	0.813	0.923	\vdash	0.994	0.814	0.821	0.819	
		20 °C	0.941	0.9261	0.9573	1.041	0.161	1.62		1.397		696.0	0.990	1.002	1.028		1.022	1.019	1.031		0.946	0.956	696.0	0.980	\vdash	0.987	966-0	⊢	
CTAB [mol kg ¹]				0.7	6 0	1.1	\vdash	1.47				50	0.7	6 0	1.1	EI	1.47	1.62	1.77		50	0.7	6 0	11	\vdash	1.47	⊢	1.77	

Table 9: Apparent molar volume, $\phi_{\rm v}$ (m³mol⁻¹) for Quercetin (1-3 mM) with different concentrations of CTAB (0.5-1.77 mM) and water-ethanol at five different temperatures

		40.C		51.91361	36,852.09	28.84110	23.56814	19.95000	17.58156	15.92400	14.57454		\$2,55779	37/31105	29.19898	23.89015	20.15276	17.80028	16.12232	14.73786		53.20526	37.77235	29,55865	24.18446	20.21481	18.09733	16.32165	14.93849
		32.52		54.89540	36.67063	27.81671	24.06527	20125895	17.57103	15.55147	14.05526		54.89540	27.12721	28.16832	24.35957	20.48735	17.78903	15.74730	14.23359		55.88286	37.58624	28.52170	24.65538	20.73701	18.00814	15.94412	14.23359
100% viv ErOH	(00% viv Efc	3.00		52,44145	36.43279	27.63527	23.76439	19.98530	17.34918	15.45018	13.87505		51.00573	36.88714	1128671	24.79316	18160.00	17.56554	15.64503	14.22994		53.89363	37.34378	1496538	25.09048	20.47957	17.78299	16.23549	14.22994
ſ		3.S		32.22748	22.63344	17.75393	14.77243	12/29/31	10.85152	9.835139	8.989459		52.24315	37.05363	28.31740	22.88191	19.72636	16.90898	15.15047	13.95474		52.88407	37.54527	28.66990	23.16887	10179.01	17.12263	15.44019	14.13173
		20.C		31.12124	1830615	17.88791	14.14624	11.86704	10.49470	9.440611	7.024296		36.60660	22.42117	20.96408	16.63959	13.97186	12.35612	11.12572	7,312185		41.47775	22.42117	24.19032	19.25398	16.29189	14.30778	12.53228	8.791612
		3.01		55.49761	39.17046	30.46601	21.87119	18.38672	15.42266	13.99468	9.526371		26.21858	18.72767	14.42209	11.79996	9.934898	8.918155	8.036429	7.333467		26.21858	18.54257	14.40771	11.76468	9.954791	8.786011	8.092438	7.333467
		3.50		30.0272	20.4990	16.0907	13.2857	11.2418	10.0322	9.18556	8.40716		30.2948	21.4481	1797.21	13.0449	135011	9,85163	9.02132	8,25683		29.7602	21.0672	15.5049	12.8053	10.8353	9.67188	8.85783	8.10720
10% v/v ErOH		3.00		31.13509	18.84958	16.40645	10.83459	10.85087	9.685416	8.145112	8.04389		31.13509	19,21937	16.70208	11.76108	11.0532	9.864757	8.465415	8.267563		25.61708	18.84958	16.70208	11.76108	10.85087	9.685416	8.145112	8.118277
		3.S		26.67133	18.62395	13.82115	12.71388	9.764597	8.896859	7.757144	6.534606		27.18904	20252.61	14.81759	12.59527	10.45757	9.072151	8.232175	7.461694		26.41336	18.68295	14.38361	12.24108	9.96147	8.80951	7.835868	7.316442
		20.C	(W	26.91249	1858581	14.66525	11.88219	8.405697	7.436309	6.671675	5.48615	(m	26.39713	18.67178	17.88791	11.99892	10.05422	8.804385	7.989202	7.312185	(W	26.91249	18.67178	18.18908	12.23317	10.25199	8.978885	8.147544	7.457109
		3.01	bercetin (lmM	13.48189	13.00608	8.788747	5.083426	6.054638	5.381017	3.455227	3.50572	bercetin (2mM)	18,20835	1/66711	7.490109	8.276739	4.30565	7.024195	4.161344	4.469047	bercetin (3mM)	8.91446	6.432971	4.833175	3.795917	3.316644	3.222244	2.930364	2.938552
_		35.0	ð	14.56312	8551576	6.182172	1.791825	0.636039	5,916118	3.925305	2,2036	ő	10.45359	7.466958	6.182172	4.54867	3.677746	4.248075	3.365219	-0.61603	δ	0.629707	0.449895	0.236974	0.751617	0.556996	-0.40338	111856'0	1.232811
30% v/v ErOH		30.02		14.17026	11.6228	10.90222	8.589637	7.641421	7.09074	6.35844	5.134338		13.70877	9.627502	7.233637	4.282675	4.832416	3.431188	3.11352	3.165689		-0.28172	0.23133	0.745131	2.025333	1.551963	1.58743	1.571153	1.139957
ľ		2.S		11.93843	51563074	7.772869	6.15082	4.505159	4.060942	3.754751	3.952496		9.262161	5.678067	3.692973	2.926524	10599017	1.827384	1.397406	1.279013		2.238316	-0.2865	\$6555.0-	1.017616	-0.2311	0.62191	0.31243	0.807427
		20.C		9.283334	19985518	10.52128	7.420424	1.915046	4.066224	4.180352	5.146887		3.92981	2,509616	1.03582	0.754706	0.717218	0.4263	0.449653	0.354107		1.639916	1.185759	15527610	0.754706	0.638653	0.564837	0.324196	0.239513
		10.C		-0.809	0.10201.0	-0.11239	-0.18395	0.63848	0.77606	0.26483	0.47487		0.24444	-0.11563	0.59035	0.76389	0.40531	-0.19258	-0.17471	-0.21688		-0.16203	1.05280	0.24921	0.20397	0.17264	0.22220	0.32813	0.35841
		35.C		-0.82599	0.087149	-0.12318	-0.19241	0.620215	0.759009	0.226049	0.458203		0.020602	-0.56121	-0.21286	0.751617	0.715245	0.283765	0.574033	0.467245		0.020602	2.06796	0.349999	0.193954	0.242419	0.283765	0.447044	0.467245
0% v/v ErOH		30.C		-1.50161	-1.0566S	-0.84511	-0.32862	0.210464	1/6661.0	0.118911	0.131761		-0.05031	-0.05726	-0.04446	0.795981	0.673579	0.248327	0.477297	0.436879		-0.05031	-0.05726	\$6531510	0.51687	0.437407	0.317526	0.351077	0.494816
		2.S		-2.42468	-3.16194	-1.814	-1.2501	-1.40522	-0.83116	-1.13954	7779.0-		-0.40124	0.255376	-0.66631	0.737938	0.624465	0.4\$2\$11	0.43814	0.343454		-0.60145	0.000361	0.449287	0.459953	0.389247	0.275214	0.31243	0.401041
		20.C		0.402611	0.172616	0.24623	-0.14539	-0.14604	-0.19706	0.000361	-0.01664		3.721351	1331664	0.583262	0.959222	\$50653.0	0.634316	0.512571	0.469164		1.864184	1.624362	1.149531	0.662044	0.403909	0.564837	0.449653	0.152359
CTAB	[mol kg' ¹]			50	6.0	60		2	147	1.62	177		50	0.7	60	=	2	1.47	1.62	1111		50	£10	60		1	1.47	1.62	171

Table 10: Apparent adiabatic compressibility, ϕ_k (m³mol⁻¹TPa⁻¹) for Quercetin (1-3 mM) with different concentrations of CTAB (0.5-1.77 mM) and water-ethanol at five different temperatures

	40.C		\$2948.9	57359.2	29253.8	13759.3	2,20001	17626.0	15951.4	14625.9		53935.5	38029.0	19798.6	24587.9	20630.8	1821333	16483.0	15091.1		59505	39298.4	30792.0	2,909.5	21084.4	1.61681	1703377	15618.7
	35.C		54625.8	37897.6	26874.9	23466.5	19668.6	16982	15011.9	13552.8		55601.9	37086.9	27768.0	24236.8	20314.7	17541.6	15509.8	14003.7		57844.7	38318.4	28692.8	25034.3	2,63902	18121.1	16025.4	14254.8
100% viv ErOH	30.0		1122112	336955	1,6925.1	23430.7	1.141.61	17020.3	15074.4	13510.4		50918.6	2,98895	27825.0	25104.7	20401.1	178871	15576.4	14174.7		\$2873.6	36148.3	1735.2	24602.0	19688.9	16922.7	19813	13323.0
8	3.S		2515.9	17594.5	13672.2	11433.2	9440	\$2,295.55	7507.31	6822.68		51477.2	36370.8	27586.7	22188.6	19228.0	16315.4	14612.9	13469.8		33175.6	37571.1	18500	1.974.7	19863.6	16857.8	15214.6	13918.4
	20.C		25064.3	14025.6	13947.4	10938.2	01116	80.5.08	7168.98	5189.89		30690.6	176163	16992.4	13965.0	11728.2	10427.9	12/11/9	5876.58		1,46058	17910.1	20421.3	16833.6	14263.4	2,672,1	1097.9	7352.54
	40.C		1384867	27502.98	21370.71	14938.46	12523.37	10383.89	9436.098	6103.586		16156.12	1150138	111.60SS	7229.536	6075.547	2303,252	4881.807	4449.493		16396.44	11543.65	685.0568	6857151	6179.402	5582,452	4992.452	4515.2
	38.C		19469.2	13178.7	10357.8	8626.44	1200.51	6399.18	17.2262	-		19374.2	-		817188		\vdash	5720.51	5275.04		1.60/31	13193.2	⊢	8026.19	6706.77	6145.88	\$93.65	5091.43
1010 AVA BLOH	30.0		20135	11932.7	10482.6	6953.60	6884.07	6146.60	5117.83	5083.65		20459.5	12378.6	10857.3	7509.06	7134.33	6284.15	\$330.85	5243.04		16158.5	11932.7	10696.2	197161	6884.07	6137.46	5124.99	5128.93
F	15.C		17463.0	12067.1	9874788	\$249.54	6233.24	5675.40	4909.44	4329.60		181165	12656.9	9681.52	8971873	6831.13	200028	5325.06	4806.74		1774.5	12067.1	08/8026	7906.62	6373.31	5613.32	4964.87	4702.50
	20.C	(T	8,02181	12575.7	952535	7682.70	5304.92	4674.11	4166.37	3334.882		18018.7	12427.8	12098.4	16:0597	6465.17	5702.60	5162.25	4714.60	(7	18129.8	12239.4	12144.8	7702.06	6508.85	5741.59	5197.64	4746.99
	40.C	Quercetin (1mM	1970109	10,2665	1976665	2966.38	19:6112	2451.98	1834.54	1706.44	Duercetin (2mM	\$\$56.79	5386.09	3918.62	3877.34	2993.68	2409.74	1946.83	1410.95	Quercetin (3mM	2731.63	2044.24	1598.16	1393.53	1357.55	1233.59	1223.06	1194.39
	35.C	æ	6371.43	4179.01	2666.58	2745.33	2618.52	2614.64	1694.37	930.210	B	4717.14	363355	2774.02	2014.73	1927.27	1900.18	1486.95	-255.092	පී	255.104	181.445	175,259	150.475	124.887	131.063	121.143	507.256
30% n'n ErOH	3.00		6332.43	5239.90	4960.56	3369.25	3457.51	\$220.99	2875.23	2280.74		6535.40	4508.30	3326.55	2918.04	2207.00	1563.56	1450.51	1428.45		556756	511.517	360.379	191.951	263.319	112.852	169119	153.194
*	2.S		15.0122	3458.96	3405.28	2676.02	1935.86	1746.84	1613.23	1504.94		4657.12	2814.33	1818.89	1438.73	1006.97	894,550	107.X19	621.311		0/6'606	711.84	633.221	410.879	318.920	202022	125.651	127,999
	20.C		3942.83	3676.21	3465.97	3247.86	1920.77	1798.77	1745.69	1254.79		1667.76	1060.98	433.478	313,999	299.858	177.198	167.613	147.403		\$16.395	581.133	452,435	364.964	307.187	269.494	154,490	0.01135
	40°C		579.623	48.2493	-53,1516	-86.456	207.017	371.497	125.817	226.519		115.048	-54,4119	279.455	366.365	195.473	-91,2558	SSS23-	-102.282		1406.57	496.585	116.940	96.6429	\$1.5013	105.245	155.945	170.273
	32.58		100'665-	41.6411	603335-	-91.7263	296.255	358,105	106.636	207.556		9.82690	-266.614	-101.213	176-655	342.856	135.188	275.836	224.335		8617.6	111.1780	165.323	91.4402	114.719	134,294	213.009	223.635
0% viv ErOH	3.00		96172-	530.744	-412.012	-159.433	101,187	96.0485	56.8106	62,8050		-38.2607	6617.17	-21.1605	\$96'185	322.646	11835	210.012	209.619		910538-	-27.4134	249.416	248.558	210.520	151.954	166.570	238.742
	15.C		517911-	-1541.13	817.108	-625.184	SC:039-	-405.616	-550.663	-443.844		-199.755	144.015	-330,105	570.874	313.045	240.399	216360	168.490		288.456	0.17310	216.136	221.551	187.831	131.621	150.108	193.244
	0.0Z		198,538	84.6775 84.6775 121.255 -71.2455	-96.187	0.17670	-8.16725		1840.50	105,559	284.763	1667114	422.956	312.297	252334	230.361		5447.56	\$17.785	578.146	332.059	201.664	281.241	221.821	89.1148			
CTAB [molkg] ']			2	1.0	60		2	147	1°0	11.1		50	10	60	11	n	1.47	1.62	111		50	10	60	=	2	147	1.62	11.1

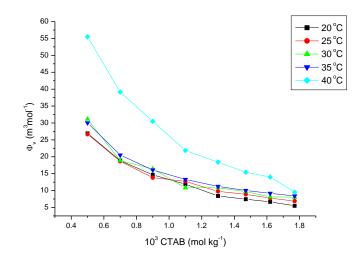


Figure 10: Graph representing Apparent molar volume (ϕ_v) vs. CTAB concentration in 70% v/v ethanol solution containing 1mM Quercetin at different temperatures

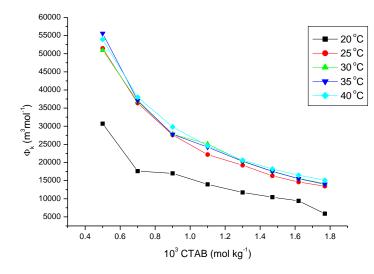


Figure 11: Graph representing Apparent adiabatic compressibility (ϕ_k) vs. CTAB concentration in 100% v/v ethanol solution containing 1mM Quercetin at different temperatures

The values of overall system in varied hydro-ethanolic concentrations have been observed to be positive. With increase in CTAB concentration, decrease in values have been observed assuring the presence of electrostatic interactions resulting in making the system more incompressible. Presence of strong hydrophobic interactions and solute-solvent interactions has been confirmed by the positive values obtained in the overall system. However in aqueous solution, uneven data has been obtained signifying the nature of interactions being unpredictable in pure water.

CHAPTER-04

CONCLUSION

4.1 Conclusion:

Physico-chemical studies including thermodynamic and thermoacoustic properties of flavonoid Quercetin has been studied in interaction with the cationic surfactant CTAB in order to study the flavonoid-surfactant interactions. The critical micelle concentration (cmc) has been observed to increase with the increasing temperature stating the major impact of solute-solvent interactions on micellization. Studies suggested that the interaction of Quercetin and CTAB are endothermic in nature. The positive values of change in enthalpy (ΔH^{o}_{m}) and change in entropy (ΔS^{o}_{m}) favoured the endothermic nature and degree of randomness for the overall system. The negative values of change in gibbs free energy (ΔG^{o}_{m}) favoured the system to proceed in forward direction. The overall study revealed that the interactions are endothermic and micellization of the system is entropically controlled. The thermoacoustic data has been used to determine the interactions within the sytem. It has been observed that at lower surfactant concentrations, the electrostatic interactions dominated the overall system whereas, on increasing the concentration of surfactant, hydrophobic interactions started dominating the system. The results obtained from apparent molar volume and compressibility studies signified that the data is consistent at hyrdoethanolic and absolute ethanolic concentration. On the other hand, no significant results have been obtained in aqueous solution. Overall, the interactions are favourable for the system to be utilised for formulation development studies and in pharmaceutical industries.

CHAPTER-05

REFERENCES

References:

- 1. Moon-Hee Choi and Hyun-Jae Shin et al. Anti-Melanogenesis Effect of Quercetin. Cosmetics. 2016;3:1-16
- K.D. Tripathi *et al. Essentials of medical pharmacology*, 4th ed. Jaypee Brothers Medical Pub. Ltd., New Delhi, 1999
- 3. F.D. King et al. Medicinal Chemistry: Principle and Practice, the Royal Society of Chem., 1984
- 4. R.S. Satoskar, S.D. Bhandarkar et al. Pharmacology and Pharmacotherapeutics-I, 11:1984
- 5. Lakhanpal P, Rai DK. *Quercetin: A versatile flavonoid*. Int. J. Med. Update. 2007;2:22–37
- 6. Takekoshi, S., Matsuzaki, K., Kitatani, et al., *Quercetin stimulates melanogenesis in hair follicle melanocyte of the mouse*. Tokai J. Exp. Clin. Med. 2013;38:129–134
- 7. Kim, Y.J. et al., *Hyperin and quercetin modulate oxidative stress-induced melanogenesis*. Biol. Pharm. Bull. 2012;35:2023–2027
- Chun, H.J., Choi, W.H., Baek, S.H., Woo, W.H., *Effect of quercetin on melanogenesis in melan-a melanocyte cells*. Korean J. Pharmacogn. 2002;33:245–251
- Chun, H.J., Hwang, S.G., Kim, C.K., Jeon, B.H., Baek, S.H., Woo, W.H. In vitro modulation of proliferation and melanization of B16/F10 melanoma cells by quercetin. Yakhak Hoeji. 2002;46:75–80
- Cho, H.W., Jung, W.S., An, B.G., Cho, J.H., Jung, S.Y. Isolation of compounds having inhibitory activity toward tyrosinase from Receptaculum nelumbinis. Korean J. Pharmacogn. 2013;44:1–5
- Fujii, T., Saito, M., Inhibitory effect of quercetin isolated form Rose hip (Rosa canina L.) against melanogenesis by mouse melanoma cells. Biosci. Biotechnol. Biochem. 2009;73:1989–1993
- 12. Nagata, H., Takekoshi, S., Takeyama, R., Homma, T., Osamura, R.Y., *Quercetin* enhances melanogenesis by increasing the activity and synthesis of tyrosinase in human melanoma cells and normal human melanocytes. Pigment Cell Res. 2004;17:66–73
- Takeyama, R., Takekoshi, S., Nagata, H., Osamura, R.Y., Kawana, S., Quercetininduced melanogenesis in a reconstituted three-dimensional human epidermal model. J. Mol. Histol. 2004;35:157–165

- 14. Matsuyama, K., Villareal, M.O., Omri, A.E., Han, J., Kchouk, M.E., Isoda, H., *Effect* of Tunisian Capparis spinosa L. extract on melanogenesis in B16 murine melanoma cells. J. Nat. Med. 2009;63:468–472
- 15. Yamauchi, K., Mitsunaga, T., Inagaki, M., Suzuki, T. Synthesized quercetin derivatives stimulate melanogenesis in B16 melanoma cells by influencing the expression of melanin biosynthesis proteins MITF and p38 MAPK. Bioorg. Med. Chem. 2014;22:3331–3340.
- Yamauchi, K., Mitsunaga, T., Batubara, I., Novel quercetin glucosides from Helminthostachys zeylanica root and acceleratory activity of melanin biosynthesis. J. Nat. Med. 2013;67:369–374
- Yamauchi, K., Mitysunaga, T., Batubara, I., Synthesis of quercetin glycosides and their melanogenesis stimulatory activity in B16 melanoma cells. Bioorg. Med. Chem. 2014;22:937–944
- 18. Taira, J., Tsuchida, E., Uehara, M., Ohhama, N., Ohmine, W., Ogi, T., *The leaf extract* of Mallotus japonicas and its major active constituent, rutin, suppressed on melanin production in murine B16F1 melanoma. Asian Pac. J. Trop. Biomed. 2015;5:819–823
- An, S.M., Kim, H.J., Kim, J.E., Boo, Y.C., Flavonoids, taxifolin and luteolin attenuate cellular melanogenesis despite increasing tyrosinase protein levels. Phytother. Res. 2008;22:1200–1207
- 20. X. Cai1, Z. Fang2, Bioavailability of Quercetin: Problems and Promises, Curr. Med. Chem. 2013;20:2572-2582
- 21. Xiao X, Shi D, Liu L, Wang J, Xie X, Kang T, et al. *Quercetin suppresses* cyclooxygenase-2 expression and angiogenesis through inactivation of P300 signaling. PLoS One. 2011;6(8):e22934
- 22. Warren CA, Paulhill KJ, Davidson LA, Lupton JR, Taddeo SS, Hong MY, et al. *Quercetin may suppress rat aberrant crypt foci formation by suppressing inflammatory mediators that influence proliferation and apoptosis.* J. Nutr. 2009;139:101–5
- Parasuraman S, Kumar E, Kumar A, Emerson S. Free radical scavenging property and diuretic effect of triglize, a polyherbal formulation in experimental models. J. Pharmacol. Pharmacother. 2010;1:38–41
- 24. Lekakis J, Rallidis LS, Andreadou I, Vamvakou G, Kazantzoglou G, Magiatis P, et al. Polyphenolic compounds from red grapes acutely improve endothelial function in patients with coronary heart disease. Eur. J. Cardiovasc. Prev. Rehabil. 2005;12:596– 600

- 25. Edwards RL, Lyon T, Litwin SE, Rabovsky A, Symons JD, Jalili T. *Quercetin reduces* blood pressure in hypertensive subjects. J. Nutr. 2007;137:2405–11
- 26. Chopra M, Fitzsimons PE, Strain JJ, Thurnham DI, Howard AN. Nonalcoholic red wine extract and quercetin inhibit LDL oxidation without affecting plasma antioxidant vitamin and carotenoid concentrations. Clin. Chem. 2000;46:1162–70
- Lamson DW, Brignall MS. Antioxidants and cancer, part 3: Quercetin. Altern. Med. Rev. 2000;5:196–208
- 28. Akan Z, Garip AI. Antioxidants may protect cancer cells from apoptosis signals and enhance cell viability. Asian Pac. J. Cancer Prev. 2013;14:4611–4
- 29. Vásquez-Garzón VR, Arellanes-Robledo J., García-Román R, Aparicio-Rautista DI, Villa-Treviño S. Inhibition of reactive oxygen species and pre-neoplastic lesions by quercetin through an antioxidant defense mechanism. Free Radic. Res. 2009;43:128-137
- 30. Johari J, Kianmehr A, Mustafa MR, Abubakar S, Zandi K. Antiviral activity of baicalein and quercetin against the Japanese encephalitis virus. Int. J. Mol. Sci. 2012;13:16785–95
- 31. Cushnie TP, Lamb AJ. Antimicrobial activity of flavonoids. Int. J. Antimicrob. Agents. 2005;26:343–56
- 32. Ramos FA, Takaishi Y, Shirotori M, Kawaguchi Y, Tsuchiya K, Shibata H, et al. Antibacterial and antioxidant activities of quercetin oxidation products from yellow onion (Allium cepa) skin. J. Agric. Food Chem. 2006;54:3551–7
- 33. Coles LS. *Quercetin: A Review of Clinical Applications*.[Last accessed: 2016 Jul 06] Ava. from: <u>http://www.chiro.org/nutrition/ABSTRACTS/Quercetin_A_Review.shtml</u>
- 34. Graefe EU, Wittig J, Mueller S, Riethling AK, Uehleke B, Drewelow B, et al. Pharmacokinetics and bioavailability of quercetin glycosides in humans. J. Clin. Pharmacol. 2001;41:492–9
- 35. Denny Joseph KM, Muralidhara, Enhanced neuroprotective effect of fish oil in combination with quercetin against 3-nitropropionic acid induced oxidative stress in rat brain. Prog. Neuropsychopharmacol. Biol. Psychiatry. 2013;40:83–92
- 36. Ferry DR, Smith A, Malkhandi J, Fyfe DW, deTakats PG, Anderson D, et al. Phase I clinical trial of the flavonoid quercetin: Pharmacokinetics and evidence for in vivo tyrosine kinase inhibition. Clin. Cancer Res. 1996;2:59–68
- 37. Suraya Jabeen, Oyais Ahmad Chat, *Investigation of antioxidant activity of Quercetin*, Food Res. Int. 2013;51:294–302

- N. A. Lipkovskaya, V. N. Barvinchenko, *Physicochemical Properties of Quercetin*, Rus. J. Applied Chem. 2014;87:36–41
- Reza S. Razmara, Ali Daneshfar, Solubility of Quercetin in Water and Ethanol, J. Chem. Eng. Data 2010;55:3934–393
- 40. Ahmet Gurses, Mehmet Yalcin a, *Mechanism of a cationic surfactant, CTAB*, Elesevier, Fuel Process. Tech. 2003;81:57–66
- 41. Martinez-Florez, S., *Flavonoids: properties and anti-oxidizing action*. Nutr. Hospitalaria. 2002;17(6):271-278
- 42. G.Pifferi, P.Restani, *The safety of pharmaceutical excipients*. I.L. Framco. 2003;58:541-550
- 43. P.J. Crowley, L.G. Martini, Drug-Excipient interactions. Pharma. Tech. 2001;05:82
- 44. Manisha mishra , P.Muthuprasanna, K.Surya prabha, P.Sobhita rani , A.Satish babu , Sarath Chandiran ,G.Arunachalam and S.Shalini, *Basics and Potential Applications of Surfactants - A Review*. Int. J. Pharma. Tech. Res. 2009;4:1354-1365
- 45. Tanaka, N., Mechanism of action of aminoglycoside antibiotics, in Aminoglycoside Antibiotics, Springer. 1982;4:221-266