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ON

"STUDIEDS ON THERMODYNAMIC PROPERTIE OF DRUG MOLECULES"

IN

CHEMISTRY

SUBMITTED TO THE UGC (WRO) PUNE

BY

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Dr. Thakur Chhaya Damodar

DECLARATION

I hereby declare that, the present work completed in the form of Minor Research Project, "**STUDIEDS ON THERMODYNAMIC PROPERTIE OF DRUG MOLECULES"**, is an original work and has not been submitted or published in any form for the fulfillment of any other degree or any other university.

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Place:
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Chapter I

Introduction:-

Physicochemical aspects of drug molecules:-

Drug-The drug is a single active chemical moiety which is found in a medicine and used for diagnosis, prevention, treatment and cure of disease. Drugs are substances meant for treatment, mitigation or prevention of diseases in human beings or other animals. Drugs are composed of organic molecules. To produce its characteristic effects, a drug must be present in appropriate concentration at its sites of action. The transfer of drugs across the biological cells or biological membrane is solely dependent on physicochemical properties of drugs. The absorption, distribution, bio-transformation and excretion of drugs involve its passage across cell membrane.

The important characteristics of drugs are their molecular size and shape, solubility at their site of absorption, degree of ionization and relative lipid solubility of their ionized and non-ionized forms. After a drug is absorbed or injected into the blood stream, it gets distributed into intestinal and cellular fluids. Patterns of drug distribution show certain physiological factors and physico-chemical properties of drugs. The drug molecule has to undergo many bio-transformations and transportations to reach at the site of action. Drug macromolecular interactions occur in physiological media important being blood intra /extra cellular fluids of membrane. Drug molecules have very complex structures and functions which are not easy to interpret. Patterns of

drugs distribution reflect certain physicochemical factors and physicochemical properties of drugs.

The physicochemical aspect of drug design involves the attainment of effective drug concentration at site of action. The drug molecule has to undergo many biotransformation and transportations to reach at the site of action. Obviously drug macromolecular interactions occur in physiological media, the important being blood intra-extra cellular fluids and membranes. The mechanisms of these molecular processes are not yet clearly understood. Bio-molecules have very complex structures and functions which are not easy to interpret. It is generally difficult to carry out direct studies on physiological media. The major constituent of body, also of body fluids is water and it is very essential to understand characteristics of water.

One of the well accepted and appreciated approaches to study molecular interactions in fluids is the use of thermodynamic methods. Thermodynamic properties are generally convenient parameters for interpreting solute-solvent and solute-solute interactions, in solution phase. Fundamental properties, such as enthalpy, entropy and Gibbs free energy represent the macroscopic state of system as an average of numerous microscopic state at a given temperature and pressure. The higher derivatives, like partial molar volume which is pressure derivative of free energy function, electrostriction, hydrophobic interaction, micellization and co sphere overlap during solute-solute interactions have been derived and interpreted from the partial molar volume data of many compounds.

The compressibility property which is the second derivative of Gibbs energy is sensitive indicator of molecular interactions with partial molar volume data.

Biopharmaceutics is an area of pharmaceutical technology dealing with the biopharmaceutical aspects of drugs are any therapeutic moiety such as it deals with the absorption, distribution, metabolism and excretion of drugs, affecting the clinical response of the drug. Usually, we specify it as MADE of the drug, which discloses the pattern, which the drug faces when ingested as dosage form. This discipline involves the complete understanding of physical, chemical, pharmacokinetic, and toxic kinetic factors, which are likely to affect the ADME profile of drug molecules. All these factors when governed thoroughly leads to effective therapeutic concentration of the drug in the biological fluids thus a desirable action is seen. Therefore, biopharmaceutics involves the study of the relationship between the physicochemical and biological factors affecting the in-vivo behavior of the drug molecules. The complete knowledge of these variables not only help in designing the drug delivery systems but also helps in generating the sub-therapeutic, therapeutic and toxic concentration of any drug in biological fluids. Not only the conventional dosage forms are designed but the novel drug delivery systems are also based on the biopharmaceuticals aspects of the known therapeutic drugs.

In general, for any drug molecule to be active pharmacologically, it should have sufficient aqueous solubility for dissolution, optimum oil or water partition coefficient to provide diffusion through lipids and protein layers and should have an active chemical group that could interact with receptor site. But such ideal

characteristics are not present in any drug molecules thus require chemical modifications.

For any clinical response the drug moiety should bear certain physical characteristics like particle size, particle form, solubility, partition coefficient and theology. Also certain chemical characteristics like coefficient surface, effect of temperature, hydrolysis, oxidation etc. are to be explored. Once physical and chemical characteristics are expressed clearly, the biological factors like gastric emptying; gastric pH, diet and glomerular filtration are screened for clinical efficacy.

It is reported that during drug protein binding, anesthesia, perceptible thermodynamic changes occur in drug. During the process of anesthesia, volumetric changes occur in drug containing membranes. The respective drug causes expansion in belayed system up to a critical volume level resulting in diminuration of nerve conductance. With the knowledge of volumetric behavior of drug an appropriate mechanism of action can be established. In case of drug protein binding anomalous, behavior of some drugs has been noted and there is need to further investigation molecular interactions.

Aim of the research problem:

Most of the research work in synthetic chemistry is dedicated in developing new molecules which are likely to prove boon to mankind. The selectivity of drug mainly depends on its bioavailability characteristics. To produce the pharmacological or therapeutic effect, the drug must reach its site

or sites of action in a concentration sufficient to initiate a response. The concentration achieved will depend on the extent and rate at which the drug is absorbed from its site of administration and its distribution by blood stream. Various physicochemical interactions occur in this process. The ultimate biological effect is sum total of physicochemical properties of drugs. The recent trend is to correlate physicochemical properties to their therapeutic effect. The first stage in this process is to study thermodynamic properties of drugs. Literature survey reveals that very few molecules are studied on this background.

Physico-chemical properties- The solute structures in a solvent media can be substantially different from their structures in their pure form (either in solid, liquid, or gas phase). The structural changes are primarily due to some interactions occurring between solvent-solvent, solute-solvent and solute-solute molecules. The greater the interactions, the more non-ideal the system behaves. These interactions can be noticed from the measurements of some bulk physico-chemical properties such as volume, refractive index, relative permittivity, enthalpy, viscosity, surface tension, speed of sound, dipole moment, etc. To study the various physico-chemical properties of drug molecules, it is first necessary that one must first investigate the properties of each component in aqueous medium and then proceed for more complex system. One of the well accepted and appreciated approach to study the molecular interactions in fluids is the use of thermodynamic method. The properties like apparent and partial molar volume, adiabatic compressibility,

viscosity, density, ultrasonic velocity and dielectric properties have proven to be very useful tools in elucidating the structural interactions occurring in aqueous and non- aqueous solutions. Studies of the partial molar volumes of electrolytes have been used to examine ion-solvent, ion-ion and solvent-solvent interactions. The apparent molar volumes of several electrolytes have been measured and the data have been used to find hydration numbers of several cations and anions. The physical property like fluidity has also been used by several workers to understand water structure modification due to addition of polar and non-polar solutes. The pioneering paper of Kaminsky has inducted new approach to this type study. Iqubal et.al. studied partial molar volumes of some drugs in water and ethanol. Chalikion et.al studied partial molar characteristics of glycine and alanine in aqueous solutions at high pressures calculated from ultrasonic velocity. The measurements of sound velocity of electrolytes and non-electrolytes in water are of comparatively recent origin. The dielectric properties of solutions are also being used by several workers to deal with the various aspects of solution chemistry.

The main objectives of our investigation are to find the thermodynamic/physicochemical properties of Phenobarbital sodium drug molecules such as 1) Partial molar volume 2) Viscosity B-coefficient 3) Molar refraction 4) Adiabatic compressibility. All these parameter will be very useful in physiological media and medical field. Such physicochemical properties are useful for the researcher and direct or indirect to the societ

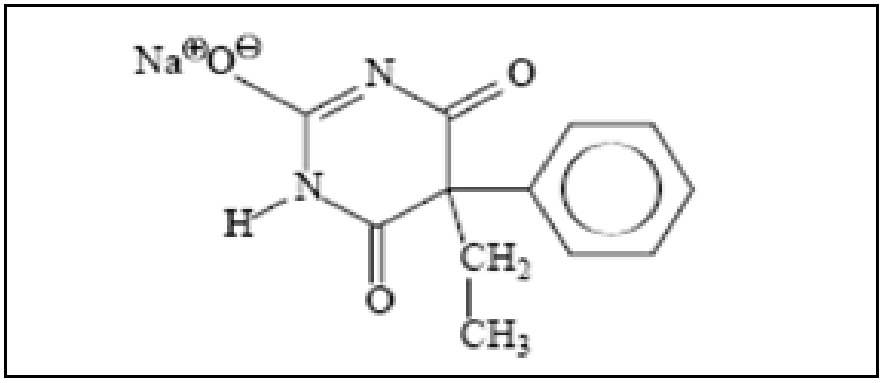
2.Drug Profile

Phenobarbital Sodium (PBS)-

Molecular formula- $C_{12}H_{11}N_2O_3.Na$

Molecular weight- 254.235 g/mol

Structure-



IUPAC name- Sodium-5-Ethyl-5-phenyl-1,3-diazinane-2,4,6-trione.

Category- Sedative, anticonvulsant.

Solubility- It is freely soluble in water and in ethanol but practically insoluble in Dichloromethane.

Description- Phenobarbital Sodium contains not less than 99.0% and not more than 101.0% of $C_{12}H_{11}N_2O_3.Na$ calculated with reference to the dried substance. It is white powder or crystalline granules. It is hygroscopic.

Uses-

Sodium Phenobarbital is a sedative, hypnotic and anti-epileptic drug. In appropriate doses, it is used in the treatment of neuroses and related tension states when mild, prolonged sedation is indicated, as in hypertension, coronary artery disease, functional gastrointestinal disorders and pre-operative apprehension. In addition, it has specific use in the symptomatic therapy of epilepsy, particularly for patients with generalized tonic–clonic seizures (grand mal) and complex partial (psychomotor) seizures. Phenobarbital is also included in the treatment and prevention of hyperbilirubinaemia in neonates. Because of its slow onset of action, phenobarbital is not generally used orally to treat insomnia but is used to help withdraw people who are physically dependent on other central nervous system depressants. Sodium phenobarbital, because it is soluble in water, may be administered parenterally. It is given by slow intravenous injection for control of acute convulsive syndromes.

Prescribed Dose-

The usual adult oral dose of Phenobarbital sodium as a sedative is 30–120 mg in two to three divided doses, that as a hypnotic is 100–320 mg and that as an anticonvulsant is 50–100 mg two or three times a day,and that as a post-operative sedative is 32–100 mg. The usual paediatric dose of sodium phenobarbital as an intramuscular sedative is 60 mg three times a day.

Side Effects-

Sedation and hypnosis are the principal side effects (occasionally, they are also the intended effects) of Phenobarbital sodium. Central nervous system effects, such as dizziness, nystagmus and ataxia are also common. In elderly patients, it may cause excitement and confusion, while in children, it may result in paradoxical hyperactivity. Another very rare side effect is amelogenesis imperfecta. Phenobarbital Sodium which is metabolized by the CYP450 enzyme system will decrease effectiveness because of faster clearance from the system. Of anticonvulsant drugs, behavioural disturbances occur most frequently with clonazepam and phenobarbital.

Chapter II

EXPERIMENTAL TECHNIQUES AND RESULTS DISCUSSION

1. Density Measurements:

Experimental- In the present work densities of drug Phenobarbital Sodium in aqueous solution having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, 0.1M at different temperatures of 25^0C, 30^0C, 35^0C and 40^0C were measured with Anton Paar Densitometer at School of Chemical Sciences, North Maharashtra University, Jalgaon. To have the more accuracy in the measurement, at each time the density of air was measured before the reading of sample solution. The density of air was found to be in the range of 0.001140 to 0.001148 gm/cm^3. The density of standard solvent (distilled water) was also measured at different temperatures and is found to be very close to the literature values

Table no.1. Density (gm/cm^3) of Water at different temperature

Sr. No.	Temperature (k)	Observed value (gm/cm^3)	Literature value (gm/cm^3)
1.	298	0.997042	0.997045
2.	303	0.995629	0.995647
3.	308	0.994369	0.994032
4.	313	0.992548	0.992216

Table no.2 Density (gm/cm^3) of Phenobarbital Sodium at different temperature.

Concentration (M)	298 K	303 K	308 K	313 K
0.02	0.999029	0.99623	0.995973	0.994135
0.04	0.999735	0.996936	0.996237	0.995728
0.06	0.999832	0.997343	0.997148	0.996749
0.08	1.000102	1.00009	0.998276	0.997357
0.1	1.005062	1.003568	0.999989	0.999958

Table no.3. Apparent Molar Volume (Φ_V) of Phenobarbital Sodium at different temperature

Concentration (M)	298 K	303 K	308 K	313 K
0.02	133.2792	203.0726	152.896	154.0329
0.04	165.3993	200.3608	186.5857	153.8817
0.06	186.286	204.5625	186.9712	163.4363
0.08	194.5605	177.2472	184.4361	173.4148
0.1	152.4861	153.516	177.0319	159.3122

2. Viscosity Measurements:

Introduction-

It is a general property of fluids (liquids and gases) to flow under an applied force. When a liquid flows through a tube, a layer of the liquid in contact with the wall of the tube remains stationary whereas the layer in the centre has the highest velocity. The velocity of different intermediate levels increases continuously with the distance from the wall of the tube to the centre. Thus there is a movement of different layers over one another in the direction of flow. This relative movement of different layers experiences a frictional force and each layer exerts a drag on the next layer in the backward direction. This internal friction or resistance which retards the flow of the liquid is known as viscosity. The common units of viscosity are poise, centipoises, and millipoise.

Experimental:

The common method used for the measurement of viscosity is the observation of flow of liquid through a capillary tube having a small diameter. The viscosity of a liquid is measured with respect to other standard liquid, generally water. In this method the flow time of equal volumes of two liquids through the same viscometer is measured. The apparatus generally used for the measurement of viscosity is Ostwalds viscometer.

In the present work specially designed **Mansingh Survismeter [Central University Gujrat]** was used to measure the flow time for standard solvent water and drug Phenobarbital Sodium. Aqueous solution of Phenobarbital Sodium having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, 0.1M were prepare in double distilled water and flow time was measured at two different temperatures of 30^0C and 35^0C **.**

Table no.4. Flow time for water at different temperature

Sr. No.	Temperature (K)	Trial-I (sec.)	Trial II(sec.)	Trial III(sec.)	Mean value (sec.)
1.	298	193.67	193.67	193.67	193.67
2.	303	183.05	183.07	183.06	183.05
3.	308	176.72	176.74	176.70	176.72
4.	313	169.58	169.58	169.58	169.58

Table no.5. Flow time (in seconds) of Phenobarbital Sodium at different temperature

Sr. No.	Temperature (K)	0.02M	0.04M	0.06M	0.08M	0.1M
2.	303	208.32	210.36	212.48	214.14	216.31
3.	308	198.52	200.53	202.40	204.16	206.28

By measuring the flow time for water and Phenobarbital Sodium, viscosity and relative viscosity of Phenobarbital Sodium is calculated.

Table no.6. Viscosity (in centipoises) of Phenobarbital Sodium at different temperature

Sr.no	Concentration (M)	303K	308K
1.	0.02	0.9075	0.8087
2.	0.04	0.9169	0.8168
3.	0.06	0.9261	0.8255
4.	0.08	0.9358	0.8337
5.	0.1	0.9479	0.8439

Table no.7. Relative Viscosity (in centipoises) of Phenobarbital Sodium at different temperature

Sr.no	Concentration (M)	303K	308K
1.	0.02	1.138	1.124
2.	0.04	1.150	1.136
3.	0.06	1.161	1.148
4.	0.08	1.174	1.159
5.	0.1	1.189	1.173

3.Refractive Index Measurements:

The refractive index of a substance is defined as the ratio of the velocity of light in vacuum to its velocity in the given medium. It is one of the physical constants that can be used to describe a chemical species. Further, it is useful for the identification of crystalline substance. Refractive index is a property of the material and is extremely useful in chemical analysis and process control. The determination of the oil content of oil bearing seeds is an interesting application of refractometry. It is a convenient and precise tool to determining the sulfur content of rubber. It is also applicable in the determination of the efficiency of distillation columns. Refractive index is an additive property Refractive index measurements are useful for the control of manufacturing processes such as in the fermentation industries, in dyestuffs and in the canning and preservation of foods, and also useful for identification or assaying some solid, liquid or constituent of a solution. It also offers a positive means for the identification of crystalline substances.

Specific and molar refractions have proved useful for analytical purposes since they are found to vary in a systematic way within homologous series of compounds. The molar refraction has been useful in structural studies. The molar refraction increases in regular increments with the number of carbon atoms within a homologous series. So, molar refraction of the compound can be considered as the sum of atomic increments and that, within certain limits, the contribution of each atom is the same in every molecule. Literature survey shows that much work has been done in liquid mixtures but very less work has

been reported for the solutions of organic, inorganic, polymeric and drug molecules. Many workers have been reported refractive index of oils, amino acid, carboxylic acid, polymer, liquid crystals and other materials etc.

In the present work efforts have been made to determine the refractive index of some drug molecules in aqueous solution having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, 0.1M at different temperatures of 25^0C, 30^0C, 35^0C and 40^0C. Refractive Indices measurements were made on Abbe refractometer [make-optics technology, no-]. The instrument is capable of determining refractive indices in the range of 1.300 to 1.700. The temperature was maintained by circulating water through jacket round the prisms of refractometer from an electronically controlled JULABO thermostatic water bath (NOVA NV-8550 E). The uncertainty of temperature was ± 0.01°C. Attaching a thermostat to this instrument, the refractive indices within the range of temperature 0°C to 70°C can be measured. The refractive index was measured by using Na- vapour lamp with wavelength of D-line of Na is 589.3 nm.

A small quantity of the experimental liquid is introduced between the two prisms. The reflector fitted on the base of the instrument is adjusted in such a way that a beam of light passes through the opening at the bottom of the lower prism. The eyepiece of telescope is focused on the cross-wire in its focal plane. The prism chamber is rotated by operating the milled head until the cross-wire coincides with the line of demarcation between bright and dark halves of the field of view. At this position, the reading on the scale directly gives the value of

refractive index of the liquid. The calibration of the refractometer was made by measuring the refractive indices of standard liquids viz. benzene and carbon tetra chloride at 298K. Refractive indices were found to be 1.501 and 1.461 respectively which are very close to the respective literature values of 1.5011 and 1.4607.

Refractive index of double distilled water was measured at temperature range of 25^0C (298K) to 40^0C (313K) and it was compared with literature.

Table no.8. Refractive Index of water at different temperature.

Sr. No.	Temperature (K)	Observed value	Literature value
1.	298	1.33250	1.33254
2.	303	1.33186	1.33192
3.	308	1.33128	1.33134
4.	313	1.33112	1.33124

Table no.9. Refractive Index of Phenobarbital Sodium at different temperature.

Sr. No.	Concentration(M)	298k	303k	308k	313k
1.	0.02	1.33365	1.33337	1.33325	1.3328
2.	0.04	1.3337	1.33342	1.3333	1.33285
3.	0.06	1.33375	1.33347	1.33335	1.3329
4.	0.08	1.3338	1.33352	1.3334	1.33295
5.	0.1	1.33385	1.33357	1.33345	1.333

Table no.10. Molar Refraction of Phenobarbital Sodium at different temperature.

Sr. No.	Concentration(M)	298k	303k	308k	313k
1.	0.02	47.90082	47.99882	47.99552	48.02532
2.	0.04	47.8735	47.97135	47.98933	47.95502
3.	0.06	47.87537	47.9583	47.95202	47.91243
4.	0.08	47.86895	47.83308	47.90435	47.88975
5.	0.1	47.63919	47.6738	47.8288	47.81952

4. Ultrasonic Velocity Measurements:

Introduction-

Ultrasonics is the technology of sound and science of acoustics. The frequency range of ultrasonic waves is greater than 20 kHz up to several MHz, which is beyond the audible limit. Low amplitude waves are more pronounced at frequencies between 2 to 10 MHz. The waves whose frequencies are lower than the audible limit are called infrasonics. The upper limit for gases is around 5 MHz and for liquids is 500 MHz. But, human ears do not respond to either of these frequencies. The ultrasonic technique is used for different investigations due to the following advantages:

- At higher frequencies, the high absorption coefficient values are easily measurable.

- Shorter wavelengths occur at higher frequencies so that plain wave conditions are more easily realized which are especially important for the smaller specimens.
- Frequencies associated with relaxation phenomena often fall within the ultrasonic range and therefore they can be easily focused.
- Less cost with efficiency comparable to other methods.

The era of modern ultrasonics began only in the early 20th century with Langevin's use of high-frequency acoustic waves and quartz resonators for submarine detection in 1917. From then on, slow but steady progress was made in the measurements of propagation constants of materials. Early landmarks included Pierce's quartz-driven ultrasonic interferometer in 1925 and the discovery in 1932 by Debye and Sears and also by Lucas and Biquard of the ultrasonic diffraction grating. An important event during 1930s was the pioneering work of Sokolov in 1934 on ultrasonic flaw detection. Ever since, the field has grown enormously with wide applications in science, medicine and other areas. Graff **investigated** physical, chemical and biological effects of ultrasounds on macromolecules, microorganisms and cells. Stokes **made** the first attempt in medical imaging using ultrasonics. An ultrasonic velocity study provides a lot of information on molecular interactions. Ultrasonic wave propagation affects the physical properties of the medium and hence can furnish information on the liquid and liquid mixtures. Studies on ultrasonic velocity, density, viscosity, acoustic, thermodynamic, excess thermodynamic

parameters and their deviations in binary systems have been the subject of many investigations in the recent years**.** These investigations on different systems reveal specific interactions between the molecules of the component liquids.

The study of the propagation behavior of ultrasonic waves in solids, liquids, liquid mixtures, electrolyte solutions, suspensions, polymers, soaps etc. is now rather well established as an effective means for examining certain physical properties of materials or medium, molecular interactions etc.. Ultrasonic waves with low amplitude have been used by many workers to investigate the structural and physico-chemical behaviour of pure liquids and liquid mixtures. It has been reported by many workers that, occurrence of complex formation can be explained successfully by excess parameters such as U^E, β^E, Lf^E etc. The positive values of U^E and negative values of β^E show strong interactions occurring in liquid mixtures showing the possibility of complex formation. This occurs due to the formation of discrete groups of molecules arranged into specific geometric structures which are influenced not only by the shape of molecules but also by the mutual interactions occurring between them. Lagemann and Dunbar pointed out the sound velocity approach for the qualitative estimation of interaction in liquids. A parallel measurement of sound velocity, density and viscosity of liquid mixtures allows one to obtain information about their volume, compressibility, free length, internal pressure, acoustic impedance, enthalpy and changes in their properties. Complex formations, formation of hydrogen bond, Dipole – dipole, dipole- induced dipole

interactions in solutions and their effect in physical properties of the mixture have received much attention.

The study of molecular interactions and the variations in these interactions due to structural changes have been carried out by various experimental techniques such as Infrared Spectroscopy technique, Nuclear Magnetic Resonance, Raman spectra and dielectric property measurements. But, the complete understanding of the nature of intermolecular and intramolecular interaction may not be possible by any single method. Ultrasonic methods have the added advantage of being less cost with efficiency comparable to other methods. Hence, a number of works have reported the study through ultrasonic method.

Experimental-

Measurements of ultrasonic velocities are made in liquids in order to get an idea of their chemical and physical characteristics. A large number of such measurements have been made and given in the literature**.** Three techniques namely echo-pulse, optical diffraction and interferometric technique are generally employed for the measurements of ultrasonic velocity in liquids. In the present work, the ultrasonic velocity measurements were made by an interferometric method. Ultrasonic interferometer,(Mittal Enterprise, New Delhi, Model No.F-05) working at frequency of 3 MHz was used to determine sound velocity. It consists of a high frequency generator and a measuring cell.

High Frequency Generator-

This is a high frequency crystal controlled oscillator based on modified Pierre circuit operating in the megahertz region. It is used to excite the piezoelectric transducer which is a quartz crystal fixed at the bottom of the measuring cell to produce ultrasonic waves at its resonant frequency in the experimental liquid filling the cell. To observe the changes in current, the oscillator is provided with a microampermeter and two trimmer condensers marked A and B on the back side of the generator assembly. These are used to adjust or tune the instrument so that sufficient deflection in anode current can be observed. Two controls are provided for the adjustment of micro-

amperemeter and controlling gain respectively. The detailed technical specifications are as given below:

(a) Mains voltage- 220V, 50Hz

(b) Measuring frequency- 3 MHz

(c) Glow lamp- 6.3 V, 0.3 A

(d) Fuse- 150 mA

Measuring Cell-

The coupling of the generator to the crystal is such that it prevents high-voltage breakdown and also provide a maximum transfer of power. A cylindrical metal container placed vertically and stably on a heavy metal base which also works as the coupler between piezoelectric crystal and the high frequency generator. Cylindrical container is a double walled jacket. Outer wall has provision for circulation of water or any other liquid for maintaining the temperature of the experimental liquid which is filled in this cell. A quartz crystal is fixed at the bottom of the cell. A movable metallic reflector plate graduated from outside by micrometre screw arrangement and kept parallel to the crystal is housed inside cell. A digital screen is also attached with cell to give direct micrometre reading. The measuring cell can be easily dismantled into three pieces viz. metal base, container, and reflector such that the experimental liquid can be easily poured into the cell. The transducer is coupled to the high frequency oscillator by a coaxial cable. The detailed technical specifications about measuring cell are as under:

(a) Maximum displacement of the reflector- 25 mm

(b) Capacity of liquid cell- 12ml

(c) Least count of micrometre- 0.001 mm

The calibration of ultrasonic interferometer was done by measuring the ultrasonic velocity of double distilled water. Experimental values of ultrasonic velocity of distilled water are found to be 1499.4 ms^{-1}, 1511.2 ms^{-1}, 1520 ms^{-1} and 1529.7 ms^{-1} at temperature of 298K, 303K, 308K and 313K respectively . These values of ultrasonic velocity agree closely with the corresponding standard values. The maximum estimated error has been found to be +0.08 %.

The temperature was maintained by circulating water around the liquid cell from thermostatically controlled adequately stirred water bath (accuracy + 0.1^{o}C) and covering the measuring cell along with its base with a specially made insulated jacket with a window for noting down micrometer readings. The solvent / solution were filled in the measuring cell with quartz crystal and then micrometer was fixed. The micrometer was rotated very slowly so as to obtain a maximum or minimum of anode current (n). A number of maximum reading of anode current were counted. The total distance (d) travel by the micrometer for n=20, was read. The wave length (λ) was determined according to the equation: $\lambda = 2d/n$. The sound velocity (U) of solvent and solutions were calculated from the wavelength and frequency (F) according to equation: $U = \lambda F$.

Table no.11. Ultrasonic Velocity of distilled water at different temperature

Sr. no.	Temperature (K)	Observed Value (ms^{-1})	Literature Value(ms^{-1})
1.	298	1499.7	1499.4
2.	303	1511.1	1509.7
3.	308	1520.2	1520.37
4.	313	1529.42	1529.70

Table no.12. Ultrasonic Velocity (M/S) of Phenobarbital Sodium at different temperature

Sr. no.	Temperature (K)	0.02M	0.04M	0.06M	0.08M	0.1M
1.	298	1505.43	1508.42	1511.45	1514.40	1517.40
2.	303	1523.16	1526.72	1529.12	1532.41	1535.15
3.	308	1538.18	1541.46	1544.66	1547.16	1550.27
4.	313	1547.31	1549.53	1551.62	1554.70	1557.96

Table no.13. Adiabatic Compressibility of Phenobarbital Sodium at different temperature

Sr. no.	Temperature (K)	0.02M	0.04M	0.06M	0.08M	0.1M
1.	298	4.42×10^{-5}	4.4×10^{-5}	4.38×10^{-5}	4.36×10^{-5}	4.32×10^{-5}
2.	303	4.33×10^{-5}	4.3×10^{-5}	4.29×10^{-5}	4.26×10^{-5}	4.23×10^{-5}
3.	308	4.24×10^{-5}	4.22×10^{-5}	4.2×10^{-5}	4.18×10^{-5}	4.16×10^{-5}
4.	313	4.2×10^{-5}	4.18×10^{-5}	4.17×10^{-5}	4.15×10^{-5}	4.12×10^{-5}

Conclusion:

Four thermodynamic/physicochemical properties i.e. refractive index, density, viscosity and ultrasonic velocity of drug Phenobarbital sodium are measured at four different temperature i.e. 298K, 303K, 308K and 313K. The aqueous solutions of Phenobarbital Sodium having concentration of 0.02M, 0.04M, 0.06M, 0.08M and 0.1M were prepared and they were used to study the solute-solvent interaction. From the experimental observations shows that the drug molecule i.e. Phenobarbital sodium shows the solute-solvent interactions in all thermodynamic/physicochemical properties.

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