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Physico-chemical studies on binary aqueous solutions of Anti-Viral Influenza drugs

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ABSTRACT

The ultrasonic velocity, density, viscosity and absorption have been measured for solution of Influenza Anti-Viral drugs (Amantadine and Oseltamivir) are presented at room temperature 303K. By taking measurements of Anti Influenza Viral drugs at 0.2, 0.4 and 0.6% concentrations of each solution. The aim of the study is to increase the solubility, stability, sweetness of drugs by the formation of complexation. The ultrasonic velocity, density and viscosity have been measured at 2MHz for the aqueous solutions of (i) Influenza Anti-Viral Drugs + HPMC (Hydroxy Propyl Methyl Cellulose), Lactose and $CaCl_2$ (Calcium Chloride at different concentrations at a temperature 303K.The acoustical parameters such as adiabatic compressibility (β), intermolecular free length (L_f), internal pressure (π_i), Rao's constant (R), relaxation time (τ), acoustical impedance (Z_a), absorption coefficient (α/f^2), free volume (V_f), cohesive energy and solvation number (Sn) have been computed. These properties are attributed to solute-solvent interactions through hydrogen bonding, segment-segment interaction, molecular association, polymer-solvent interaction, polymer-polymer interaction and etc. The total absorption can be considered as the sum of contributions from solute-solvent interactions. These results are further supported by FTIR studies.

1. Introduction

The ultrasonic study of an aqueous mixture is important in understanding the nature of molecular interactions. The biological activity of drug molecules and the activation energy of the metabolic process basically depend on the type and strength of the inter-molecular interactions (Bedare et al., 2014). Interaction of drugs with different additives was carried out in order to increase their properties and applications; indeed, it was found so (Dileep and Malik, 2017; Dileep et al., 2018a; 2018b; 2018c). Amantadine is an antiviral medication used to prevent or treat certain influenza infections; Amantadine shows potential for use as a safe alternative/augmenting agent for treating children with neuropsychiatric and various other disorders (Hosenbocus and Chahal, 2013). Oseltamivir is an antiviral medication that blocks the actions of influenza virus types A and B in our body. Oseltamivir is an orally administered antiviral medication that selectively inhibits the influenza neuraminidase enzymes that are essential for viral replication. Oseltamivir is suitable for use in diverse patient populations, which may include young children and elderly patients, various ethnic groups and those with renal or hepatic impairment (Brian and Davies, 2010). Now a day's Ultrasonic investigations is employed in a wide range of applications in medicine, biology, industry, material science, agriculture, oceanography, sonochemistry due to its non-destructive nature (Blitz, 1963; Suslick, 1988; Mason, 1990; Naik et al., 2015; Carncim et al., 1999; Kruger et al., 1999; Masuelli, 2018). Polymers are one of the most essential products which ambiances us in every gait of life HPMC is a polysaccharide prepared from cellulose (Arumugam et al., 1998). It contains both methyl and hydroxy propyl substitutes. In the present study, HPMC has been chosen as polymer, as they have many pharmaceutical and biomedical applications (Nithiyanantham et al., 2012). A new approach for escalating a drug–excipients mixed coat with highly water-soluble has been investigated. Studies reveal that incorporation of hydrophilic substances such as HPMC, Lactose, $CaCl_2$ with drugs itself considerably increase the release rates. An important research area involves the development of sustained delivery systems, which are designed to control the release of drugs at a special rate over a defined

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Table 1
The measured parameters Ultrasonic velocity(U), density (ρ), viscosity (η) and the derived parameters adiabatic compressibility (β, free length (L_f), internal pressure (πi_j), Rao's constant (R), absorption coefficient (α/f^2), free volume (V_f), cohesive energy (CE), relaxation time (τ), acoustical impedance (Za) and salvation number (Sn)dd for Amantadine + HPMC, Oseltamivir + HPMC, Amantadine + Lactose, Oseltamivir + Lactose and Amantadine_$CaCl_2$, Oseltamivir + $CaCl_2$ in aqueous solution at 303K.

Conc.%	U ms^{-1}	P kgm^{-3}	$\eta \times 10^{-3}$ Nsm^{-2}	$\beta \times 10^{-10} N^{-1}m^2$	L_fÅ	$\pi_i \times 10^6$ Pascal	R	$\alpha/f^2 \times 10^{-11}$ $Npm^{-1}s^2$	V_f m^3mol^{-1}	CE $\times 10^5$ $kJmol^{-1}$	T $\times 10^{-13}$ s	$Z_a \times 10^6$ $kgm^{-2}s^2$	Sn
Amantadine + HPMC													
0	1531	1010	0.912	4.224	0.410	0.883	1.462	1.012	0.011	1.123	5.135	1.546	-
0.25	1546	1042	1.024	4.015	0.399	0.409	2.928	1.081	0.028	1.039	5.480	1.610	547
0.5	1559	1051	1.052	3.914	0.394	0.240	4.659	1.082	0.056	0.967	5.489	1.638	543
0.75	1567	1062	1.086	3.834	0.390	0.166	6.447	1.095	0.088	0.924	5.551	1.664	582
1.0	1575	1070	1.121	3.767	0.387	0.125	8.275	1.110	0.125	0.895	5.629	1.685	626
1.25	1583	1078	1.167	3.701	0.383	0.101	10.108	1.135	0.161	0.878	5.758	1.706	675
1.50	1592	1084	1.198	3.639	0.380	0.083	11.961	1.146	0.203	0.861	5.812	1.725	723
1.75	1609	1091	1.246	3.540	0.375	0.071	13.822	1.159	0.242	0.850	5.880	1.755	806
2.0	1617	1099	1.295	3.480	0.372	0.063	15.636	1.184	0.280	0.844	6.007	1.777	855
Oseltamivir + HPMC													
0	1525	1007	0.894	4.270	0.412	0.874	1.465	1.003	0.011	1.116	5.088	1.535	-
0.25	1533	1028	0.971	4.139	0.405	0.396	2.959	1.056	0.030	1.021	5.357	1.575	383
0.5	1541	1036	1.012	4.064	0.402	0.234	4.708	1.081	0.058	0.959	5.483	1.596	384
0.75	1549	1045	1.053	3.988	0.398	0.162	6.527	1.104	0.091	0.920	5.598	1.618	432
1.0	1556	1056	1.095	3.911	0.394	0.123	8.351	1.126	0.127	0.894	5.709	1.643	490
1.25	1563	1063	1.131	3.850	0.391	0.099	10.207	1.145	0.166	0.874	5.805	1.661	536
1.50	1572	1074	1.174	3.767	0.387	0.083	12.022	1.163	0.205	0.860	5.896	1.688	605
1.75	1580	1085	1.205	3.691	0.383	0.071	13.814	1.169	0.248	0.845	5.930	1.714	669
2.0	1591	1094	1.241	3.611	0.379	0.062	15.623	1.178	0.291	0.834	5.973	1.740	737
Amantadine + HPMC													
0	1531	1010	0.912	4.224	0.410	0.868	1.484	1.012	0.011	1.121	5.135	1.546	-
0.25	1525	1022	0.924	4.207	0.409	0.333	3.370	1.022	0.039	0.980	5.182	1.558	336
0.5	1530	1027	0.936	4.159	0.406	0.198	5.275	1.023	0.076	0.912	5.189	1.571	320
0.75	1534	1033	0.945	4.113	0.404	0.139	7.171	1.022	0.120	0.867	5.182	1.584	339
1.0	1541	1039	0.957	4.053	0.401	0.106	9.066	1.019	0.170	0.835	5.170	1.601	384
1.25	1547	1044	0.961	4.002	0.399	0.084	10.962	1.011	0.227	0.807	5.127	1.615	421
1.50	1551	1049	0.979	3.962	0.397	0.0710	12.847	1.02	0.283	0.791	5.171	1.626	450
1.75	1554	1054	0.986	3.928	0.395	0.060	14.721	1.018	0.347	0.773	5.163	1.637	475
2.0	1559	1061	0.992	3.877	0.392	0.052	16.561	1.011	0.416	0.757	5.127	1.654	516
Oseltamivir + HPMC													
0	1525	1007	0.894	4.270	0.412	0.859	1.486	1.003	0.011	1.113	5.088	1.535	-
0.25	1519	1018	0.915	4.257	0.411	0.332	3.379	1.024	0.039	0.978	5.192	1.546	261
0.5	1526	1023	0.926	4.197	0.408	0.197	5.291	1.022	0.077	0.909	5.181	1.561	275
0.75	1532	1029	0.937	4.140	0.406	0.138	7.195	1.020	0.121	0.865	5.171	1.576	311
1.0	1538	1034	0.942	4.088	0.403	0.105	9.103	1.012	0.174	0.830	5.133	1.590	348
1.25	1543	1041	0.955	4.034	0.400	0.084	10.984	1.013	0.229	0.806	5.136	1.606	390
1.50	1548	1047	0.968	3.985	0.398	0.070	12.863	1.014	0.287	0.787	5.143	1.620	428
1.75	1553	1051	0.974	3.940	0.396	0.060	14.760	1.010	0.353	0.769	5.122	1.632	459
2.0	1557	1059	0.989	3.895	0.393	0.052	16.585	1.012	0.417	0.757	5.135	1.648	500
Amantadine + Lactose													
0	1531	1010	0.912	4.220	0.410	0.882	1.464	1.012	0.011	1.123	5.135	1.546	-
0.25	1536	1029	0.939	4.119	0.404	0.379	3.032	1.016	0.033	0.999	5.155	1.580	424
0.5	1541	1036	0.947	4.064	0.402	0.222	4.792	1.012	0.066	0.925	5.131	1.596	394
0.75	1547	1044	0.952	4.002	0.399	0.152	6.611	1.001	0.108	0.874	5.079	1.615	426
1.0	1554	1052	0.965	3.936	0.397	0.114	8.454	0.998	0.155	0.840	5.063	1.634	473
1.25	1564	1061	0.971	3853	0.391	0.091	10.298	0.983	0.211	0.809	4.987	1.659	540
1.50	1569	1066	0.984	3.810	0.389	0.075	12.168	0.985	0.269	0.789	4.998	1.672	572
1.75	1575	1071	0.996	3.764	0.387	0.063	14.039	0.985	0.331	0.772	4.997	1.686	608
2.0	1582	1076	1.116	3.713	0.384	0.055	15.909	1.089	0.392	0.761	4.524	1.702	649
Oseltamivir + $CaCl_2$													
0	1525	1007	0.894	4.270	0.412	0.874	1.466	1.003	0.011	1.116	5.088	1.535	-
0.25	1531	1021	0.914	4.178	0.407	0.396	3.053	1.004	0.030	1.021	5.090	1.563	343
0.5	1536	1029	0.926	4.119	0.404	0.234	4.819	1.002	0.058	0.959	5.084	1.580	336
0.75	1542	1038	0.937	4.051	0.401	0.162	6.642	0.998	0.091	0.920	5.060	1.600	377
1.0	1546	1046	0.949	3.994	0.378	0.123	8.490	0.996	0.127	0.894	5.053	1.618	417
1.25	1553	1054	0.956	3.933	0.395	0.099	10.342	0.988	0.166	0.874	5.013	1.636	465
1.50	1558	1063	0.961	3.875	0.392	0.083	12.174	0.979	0.205	0.860	4.964	1.656	512
1.75	1564	1069	0.976	3.824	0.390	0.071	14.032	0.981	0.248	0.845	4.975	1.671	553
2.0	1571	1074	0.982	3.772	0.387	0.062	15.901	0.974	0.291	0.834	4.938	1.687	596

period of time. Binary aqueous solutions containing soluble carbohydrates (Lactose) and electrolytes ($CaCl_2$) have been widely used in food and pharmaceutical applications (Jin et al., 1995; Vanathi et al., 2013; Nithiyanantham and Palaniappan, 2012).

The behavior of drugs with HPMC, Lactose and $CaCl_2$ in aqueous media has been examined to prove the increasing solubility and stability of the drug. At the same time, HPMC causes sustained release of highly soluble drugs; thus the role of these magical molecules in pharmaceutical chemistry has opened new avenues for research and development (Mehta et al., 2005).

As every pharmacist knew that, many pharmaceutical drugs have an unpleasant taste, often very bitter. The major consequence of the bitter taste is to restrict greatly the further development of oral preparations and clinical applications of these drugs. Along with the continuing improvement in the social standard of living, it is no longer acceptable for useful medicines to taste bitter. People wish to take effective drugs that have a nice taste and can be administered easily. Accordingly, it is important to mask the unpleasant taste of a drug in order to improve the product quality. This will also increase the value of the finished product

as well as patient compliance, especially where infants, children and elderly are concerned.

In order to achieve more pleasant dosage forms, various masking techniques have been described in the literature (Shouand and Chen, 2002; Yuan et al., 2016). Various techniques are used for the enhancement of the solubility of poorly soluble drugs which include physical and chemical modifications of drug and other methods like particle size reduction, crystal engineering, salt formation, solid dispersion, use of surfactant, complexation and etc, The simplest method is to add flavors or sweeteners. However, in most of the cases, these are rather limited and may not be effective enough to mask the unpleasant taste of some drugs. A number of more useful approaches have been tried, including capsule formulations, coating with water-soluble polymers, microencapsulation with various polymers (Loftsson and Masson, 2001; Nithiyanantham and Palaniappan, 2010), and chemical modification such as turning drugs into their milk-toast prodrugs without any reduction in bioavailability.

2. Materials and methods

The pure samples of these polymers and carbohydrate with an purity of 99.5 % are obtained from Madras scientific Chemicals, Salem. The drug gift samples are obtained from Sun plasma, Mumbai, India. The ultrasonic velocity and absorption studies are undertaken in the aqueous solutions of (i) Influenza anti-viral drugs (Amantadine and Oseltamivir) + HPMC, Lactose and $CaCl_2$ with a view to understand the nature of interaction between the two different solutes at 303K. Double distilled water is used in the preparation of experimental solution. For this different dissolved ultrasonic velocities of solutions were measured using a single frequency continuous wave ultrasonic interferometer (Model F81, Mittal Enterprises) to an accuracy of ±0.05% at a frequency of 2MHz at 303K. The temperature of the samples were maintained constant to an accuracy of ±0.1K using a thermostatically controlled digital water bath. This is the principle based on the reflection from the bottom and top of the cell. The reflection and the conversion of mechanical energy converted into electrical energy with help of piezo electric crystal (transducer) situated at the bottom of the ultrasonic cell. This will produce the standard wave pattern and it depends on the nature of liquids hold in the cell. The densities of the solutions were measured using a specific gravity bottle with an accuracy of ±0.01 kgm^{-3}. The viscosity was measured using Ostwald's viscometer to an accuracy of ±0.2%. The FTIR spectra were collected for these samples using Fourier Transform Infra-Red Spectrometer. Model: Spectrum RX, Perkin Elmer. All spectra were collected in the range (4000-400cm^{-1}). The KBr technique was used to prepare the samples for IR measurements.

3. Calculation

3.1. Physical parameters

Thermodynamic parameters such as adiabatic compressibility (β), intermolecular free length (L_f), internal pressure (π_i), acoustic impedance (z) and Solvation number (S_n) were calculated from empirical Jacobson's relations (Nithiyanantham and Palaniappan, 2010; Kazafi and Ansari, 2011).

(i) Adiabatic compressibility $\beta = 1/u^2 \rho$ (1)

has been calculated from the u-ultrasonic velocity and ρ-density of the medium using the Newton –Laplace equation.

(ii) Intermolecular free length $L_f = K_T \beta^{1/2}$ (2)

Where K_T is the temperature dependent constant known as Jacobson's constant ($K_T = 2.131 \times 10^{-6}$), and β is the adiabatic compressibility

(iii) Internal pressure $\pi_i = bRT\,[K\,\eta/u]^{1/2}\,\rho^{2/3}/M^{7/6}$ (3)

(Where, b stands for cubic packing, which is assumed to be 2 for all liquids, T-absolute temperature in Kelvin, Where M_{eff} is the effective molecular weight of the mixture ($M_{eff} = \sum m_i x_i$, where m_i and x_i are the molecular weight and mole fraction of individual constituents, respectively K is a temperature independent constant which is equal to 4.281×10^9 (Nithiyanantham and Palaniappan, 2014) for all liquids, R is the universal gas constant, η-Viscosity of the solution).

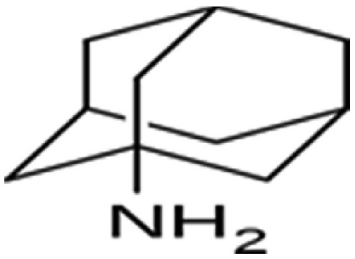

Fig. 1. Structure of Amantadine.

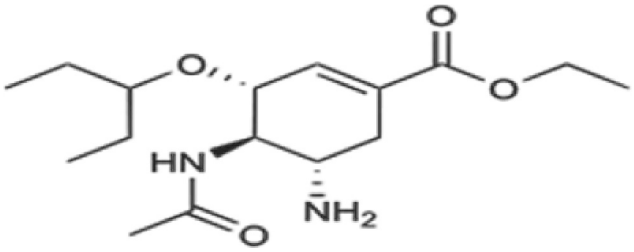

Fig. 2. Structure of Oseltamivir.

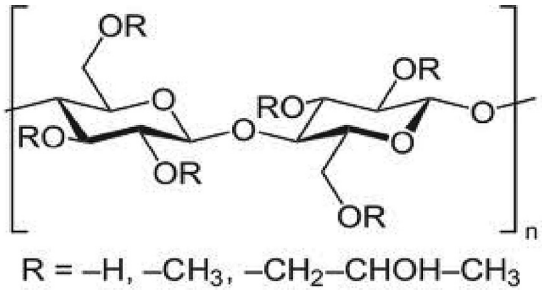

Fig. 3. Structure of HPMC.

(iv) Rao's constant $R_a = (M/\rho)\,(u)^{1/3}$ (4)

(v) Relaxation time $\tau = 4/3\beta\eta$ (5)

(vi) Acoustic impedance $za = \rho\, u$ (6)

(vii) Absorption coefficient $\alpha/f^2 = (8\pi^2\eta/3\rho u^2)$ (7)

(viii) Free Volume $V_f = (M_{eff}\, u/K\, \eta)^{3/2}$ (8)

(ix) Cohesive energy $CE = V_f\, \pi_i$ (9)

(x) Solvation number $Sn = M_2/M_1[1-((\beta)/\beta o)][(100-x)/x]$ (10)

Where M_1, $M_2$are the molecular weight of the solvent and solute, β and β_o are the adiabatic compressibility of solution and solvent.

4. Results and discussions

4.1. Influenza anti-viral drugs (Amantadine and Oseltamivir) + HPMC, Lactose and $CaCl_2$

Using the measured values of ultrasonic velocity, density and viscosity of the solutions other acoustical parameters, viz., adiabatic

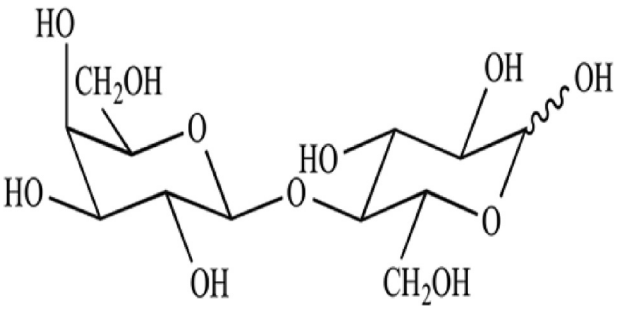

Fig. 4. Structure of Lactose.

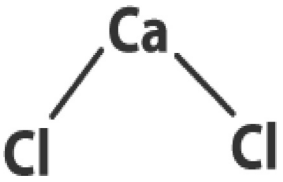

Fig. 5. Structure of calcium chloride.

compressibility, intermolecular free length, internal pressure and Rao's constant are calculated and shown in Table 1. The values of absorption co-efficient, free volume, cohesive energy, relaxation time, acoustic impedance and solvation number with concentration in the solutions and other calculated parameters at room temperature 303K are listed in the same Table.1. The chosen samples are depicted in shown in Figs. 1, 2, 3, 4, and 5.

The behaviour of sound velocity against concentration of HPMC in 1% Influenza anti-viral drugs is given in Table 1. It shows that velocity, density, viscosity gradually increases with the increase in concentration. In Influenza anti-viral drugs (1%) + HPMC, Lactose, $CaCl_2$ the sudden dip is observed adiabatic compressibility, intermolecular free length, internal pressure, absorption co-efficient, cohesive energy and relaxation time decreases with increase in concentration of solution of all the systems. From Table.1, it is further observed that Rao's constant, free volume, acoustical impedance and solvation number increases with the increase in concentration of polymer.

In the present work all the systems behave in a similar manner with respect to change in concentrations. It can be seen that the ultrasonic velocity increases with increases in concentration of HPMC, Lactose and $CaCl_2$ in 1% drug. Since the adiabatic compressibility of the solution can be obtained by measuring the ultrasonic velocity any change in hydrogen bond strength or formation of hydrogen bond will be reflected in the measured values of velocity (Rajkotia et al., 1997). From Table 1, it is observed that velocity increases non-linearly with increasing concentration of solutes. The gradual increase in ultrasonic velocity with solute concentration at 303K may be due to association between solute and solvent molecules, HPMC, Lactose and $CaCl_2$, direct segment –segment interaction will exist.

From the same Table 1, the increase of viscosity with solute concentration also confirms the possibility of molecular association (Nithiyanantham and Palaniappan, 2016). The results unambiguously show that as water concentration increases, the number of water molecules tightly connected to the HPMC, Lactose and $CaCl_2$ tends to saturate the two lone pair of each oxygen atom. Moreover, some H_2O also a strong indication that the interaction strength of the H_2O molecules bonded to the ether oxygen's are higher compared with those of the end groups (Jin et al., 1995).

Adiabatic compressibility (1) and intermolecular free length (2) decreases with an increase of solute concentration further confirm association in these systems are presented in Table.1. The adiabatic compressibility decreases with an increase in concentration of the solutes is due to the influence of electrostatic field of the ions on the surrounding solvent molecules (Majumdar et al., 1980). It may be explained on the basis of close-packing of ionic head groups in the solute resulting in an increase in ionic repulsion and finally internal pressure decreases in some systems. When the size of the solute increases, the repulsion also increases, thereby a decrease in the value of β occurs. The reduction in π_i may be due to the loosening of cohesive forces (9) which leads to breaking up the structure of the solvent (Kazafi and Ansari, 2011; Nii and Ishii, 2005; Savjani et al., 2012; Shipra and Oza, 2002).

The specific acoustic impedance (6) increases with an increase in solute concentration (Table.1). It can be explained on the basis of solute-solvent interaction between the intermolecular distance leaving a relatively wider gap between the molecules and thus becoming the main cause of impediments to the propagation of ultrasonic waves. The non-linear variation of Rao's constant (Ra) (4) and the gradual increase in acoustic impedance (Za) (6) with increase in concentration predict the strong intermolecular association complexes between the molecule of Influenza Anti-Viral drugs (HPMC, Lactose and $CaCl_2$) molecules. The increase of HPMC, Lactose and $CaCl_2$ concentration is accompanied by an increase of relaxation time (5).

From the same Table.1, the absorption co-efficient (7) values are found to decrease on the addition of solutes almost in all the system of studies. Ultrasonic relaxation processes in polymer solutions may result from viscoelasticity, polymer-solvent interaction and polymer-polymer interaction.

From the polar HPMC, Lactose and $CaCl_2$ the orientation of polar molecules in the direction of the field is faster. When solute is added to the solvent (HPMC, Lactose and $CaCl_2$ with 1% drugs), the dipole moment of this solute may cause the solvent molecule to orient in an orderly manner than before, which may cause the decrease in absorption of the solvent on adding solute. Dilute solutions contain isolated macromolecules of coiled conformation in the solvent, whose molecules are oriented near macromolecules.

When a solute is dissolved in aqueous carbohydrate or polymer solution, it can have two effects: (i) the solute act as acceptors and they can complete with protons for the lone pair of electrons on the oxygen. This leads to the formation of solution sheath around the new solute and the polymer. The equilibrium between the two structural forms in water is distributed, which leads to a change in absorption in the aqueous HPMC, Lactose and $CaCl_2$ with 1% drug solution (Geetha and Rakkappan, 2005). The concept of free volume (8) is a generalized aspect of the idea that its neighbors in a cell enclose each molecule. The free volume is broadly defined as the averages volume in which the center of the molecule can move inside the hypothetical cell due to the repulsion on the surrounding molecules.

Solvation number (Table.1) decreases and then increases with an increase in solute concentration. The values of Sn correspond to the number of solvent molecules in the primary solvation sheaths of the ions. On account of electrostriction molecule, the solvation sheath will be less compressible than that in the bulk of the solution when an external pressure is applied. The compressibility of solvent molecule near but not in the primary solvation sheath is the same as those of pure solvent molecules than that of actual primary solvation numbers. The higher values of solvation number (10) suggest a considerable dissociation of solute molecules. In some systems, solvation number increases with solute concentration, because the solutes may have two lone pairs for the interaction with the solvent molecule. The resultant values of Sn are decided by the type of interaction occurring in the solution. The decrease of Sn with the concentration indicates that solute-solvent interaction is more powerful than solute-solute interaction. The increase of Sn with solute concentration indicates that solute-solute interaction is more powerful than solute-solvent interaction in some systems.

The solute - water interaction due to hydrogen bonding is a major source ultrasonic relaxation. The mechanism should produce a linear increase in density and ultrasonic velocity and absorption with increasing concentration. The decrease of cohesive energy and increase

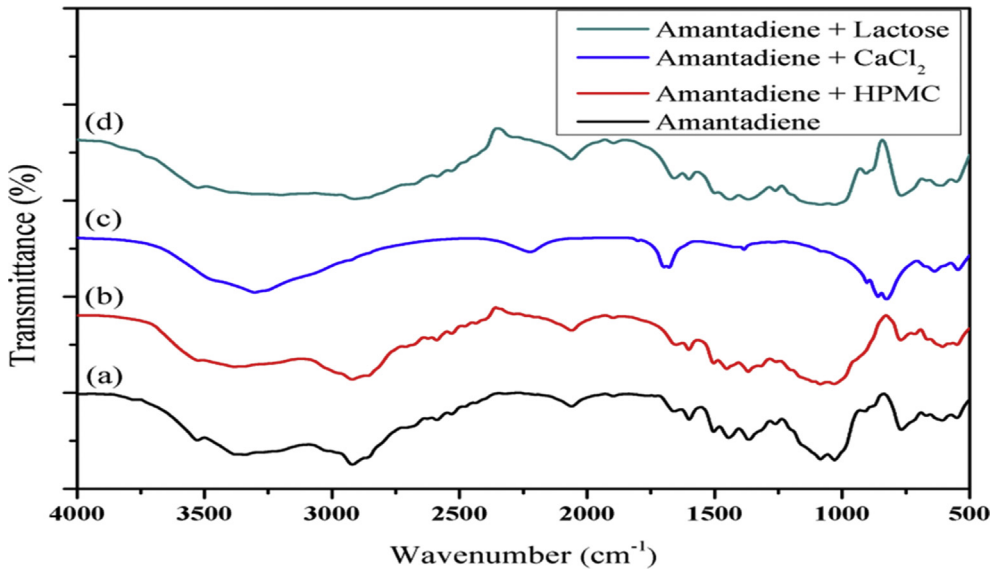

Fig. 6. FTIR spectra for a) Amantadiene, b)Amantadiene + HPMC, c) Amantadiene + $CaCl_2$,d) Amantadiene + Lactose.

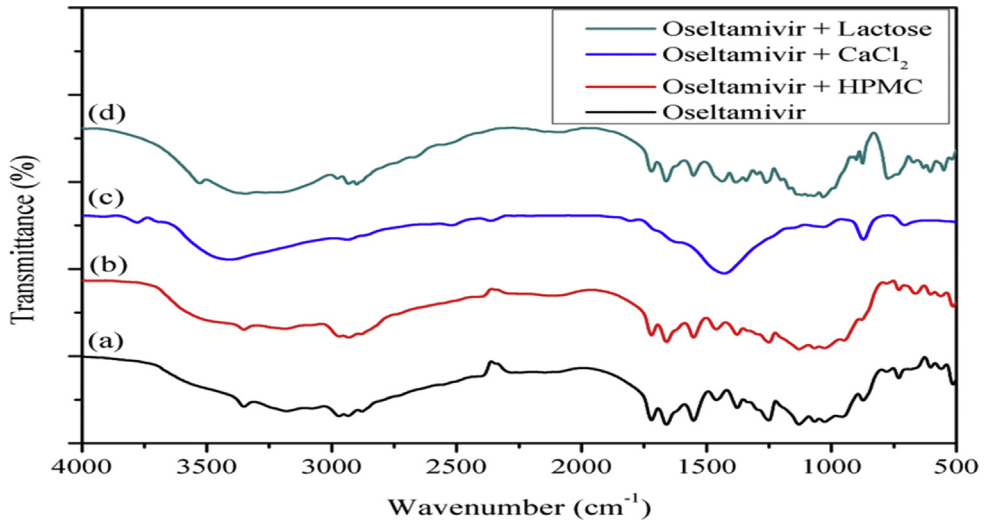

Fig. 7. FTIR spectra for a) Oseltamivir, b) Oseltamivir + HPMC, c) Oseltamivir + $CaCl_2$, d) Oseltamivir + Lactose.

of relaxation time clearly confirm the complex formation around the HPMC, Lactose and $CaCl_2$ with 1% drugs molecule which leads to a decrease in free water component.

4.2. FTIR spectra for binary mixture of influenza anti-viral drugs with HPMC, Lactose, $CaCl_2$

The characteristics peaks of Influenza anti-viral drugs with excipients of HPMC shows the broad spectrum of strong ν(OH) band. The ν(OH) band of 3341 cm-1 in Amantadine drug is shifted to 3382 cm-1 in the mixture of HPMC, but in the mixture of Lactose and CaCl2 it was about 3199 cm-1 and 3303 cm-1 and it may have interaction with the carboxyl group is displayed in Fig. 6.

The wave numbers observed in the region of 2920 cm^{-1} was assigned to C–H stretching vibration and it was shifted to 2711 cm^{-1}, 2984 cm^{-1}, 2970 cm^{-1}Amantadine(HPMC + Lactose + $CaCl_2$). The band arising at 1084 cm^{-1}due to C–N stretching of aliphatic amines was shifted to 1085 cm^{-1} in Amantadine + HPMC, Amantadine + Lactose. The IR spectrum of the entire mixture component can be shown that the interaction between two different molecules is not much more influenced. However, we can discuss the interaction in the form of hydrogen bonding. Similarly in Fig. 7 (a, b, c and d) the ν(OH) band of 3351 cm^{-1} was observed in Oseltamivir. The change in OH stretching was not observed in Oseltamivir + HPMC but small changes were observed in Oseltamivir + Lactose and Oseltamivir + $CaCl_2$ bands at 3345 cm^{-1} and 3408 cm^{-1}.

The observed level of C–H stretching vibration of 2934 cm^{-1} was shifted to 2932 $cm^{-1}$of Oseltamivir + HPMC and Oseltamivir + Lactose and 2936 $cm^{-1}$of Oseltamivir + $CaCl_2$. The strong bond of C=O stretch in Oseltamivir at 1719 cm^{-1} was observed. There was no change observed in Oseltamivir + Lactose and Oseltamivir + $CaCl_2$. Similarly the mixture also have the interaction with amino group and C=O group.

5. Conclusion

The ultrasonic velocity and absorption data for the aqueous solutions of (i) Influenza Anti - Viral Drugs/HPMC, (ii) Influenza Anti-Viral Drugs/Lactose and (iii) Influenza Anti-Viral Drugs/$CaCl_2$, the binders HPMC, Lactose, $CaCl_2$ enhance their solubility, stability and in vitro activity and it may be useful to enhance the pharmaceutical applications. Formation of complex with side chain of drugs is confirmed by FTIR studies for all

the above samples. Thus it can be concluded that experimental data and other acoustical calculations of these systems (Anti Influenza Viral Drugs + HPMC, Lactose and $CaCl_2$) shows that the solute-solvent interaction through hydrogen bonding exists in lower concentrations and solute-solute interaction may be possible due to complex formation in higher concentration. Thus above results could imply greater ability of strong interaction is between Amantadine + HPMC than other binary mixtures. In brief the solute-solvent interactions through hydrogen bonding, segment-segment interaction, molecular association, polymer-solvent interaction, polymer-polymer interaction and etc.

Declarations

Author contribution statement

S Punitha: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

R Uvarani: Analyzed and interpreted the data; Wrote the paper.

A Panneerselvam:; Performed the experiments; Contributed reagents, materials, analysis tools or data.

Nithiyanantham Subramanian: Conceived and designed the experiments.

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The authors declare no conflict of interest.

Additional information

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