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Solubility of Cholesterol in some alcohols from 293.15 to 318.15 K

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Abstract

The solubility of cholesterol in methanol, ethanol, propanol and butanol was measured by a gravimetrical method from (293.15 to 318.15) K under atmospheric pressure and the solubility data were correlated against temperature. It is observed that solubility increases linearly with increase in temperature. Solubility is higher in butanol and a minimum in methanol.

Keywords: Cholesterol, solubility, alcohols.

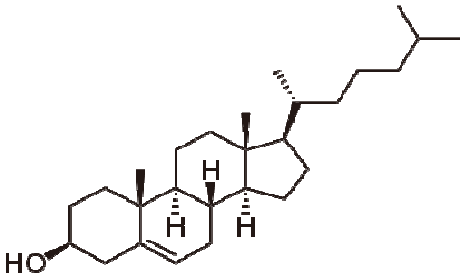
Introduction

Cholesterol is best known for the association of cardiovascular disease with various lipoprotein cholesterol transport patterns and high levels of cholesterol in the blood as shown by Weng Y. et al. It is present in higher concentrations in tissues which either produce more or have more densely-packed membranes. To build and maintain cell membranes, cholesterol is required which may also act as an antioxidant as previously shown by Smith L. Cholesterol is a sterol (a combination steroid and alcohol) and a lipid found in the cell membranes of all body tissues, and transported in the blood plasma of all animals. Lesser amounts of cholesterol are also found in plant membranes. Due to its presence in cell membrane, it participates in various types of interactions such as hydrogen bonding, Van der Waals, dipole-dipole etc.[3, 4] The hydrogen bonding and Vander Waals interactions are important for the cholesterol biological functions.

Further, the problem of cholesterol solubility in the bile and its precipitation in the gallbladder with subsequent formation of gallstones has been investigated on the basis of bile analyses [5] As cholesterol is the major component of most gallstones and it is sparingly soluble in water, [6, 7] its solubility have been studied in alcoholic solution of bile salt.[3]

In the present study, the solubilities of cholesterol in some alcohols such as methanol, ethanol, propanol and butanol have been measured from (293.15 to 318.15) K at atmospheric pressure. These alcohols display different physical and chemical properties due to the groxing number of carbon atoms in their hydrocarbon chain. The study xill screen alcohols for their utility in dissolving cholesterol and thus, cholesterol gallstones. Further, the study of interaction between cholesterol and an alcohol might, therefore, be valuable in the study of similar interactions of cholesterol in biological systems containing xater.

Figure 1: Structure of Cholesterol



Chemical Name: Cholest-5-en-3β-ol

Materials and Methods

Experimental Section

Materials. Cholesterol, xith a mass fraction purity of 99.5 %, was purchased from HiMedia Pvt. Ltd. (Mumbai, India). All the alcohols selected for the present study were analytical grade reagents which were purified by fractional distillation. Their purities were checked by SHIMADZU GC-MS (Model No QP-2010) and were found to be greater than 99.60 %.

The drug was recrystallized and its melting temperature was determined with an open capillary method. The observed value was found to be 149 °C which is in good agreement with the reported value [8] (149.8 °C).

***Apparatus and procedure*:** The solubilities were measured by a gravimetric method. [9] For each measurement, an excess mass of cholesterol was added to a known mass of solvent. Then, the equilibrium cell was heated to a constant temperature with continuous stirring. After, at least 3 h (the temperature of the water bath approached constant value, then the actual value of the temperature was recorded), the stirring was stopped and the solution was kept still for 2 h. A portion of this solution was filtered and by a preheated injector, 2 ml of this clear solution was taken in another weighted measuring vial (m_0). The vial was quickly and tightly closed and weighted (m_1) to determine the mass of the sample (m_1- m_0). Then, the vial was covered with a piece of filter paper to prevent dust contamination and placed at room temperature to evaporate the solvent. After the solvent in the vial had completely evaporated, the vial was dried and reweighed (m_2) to determine the mass of the constant residue solid (m_2- m_0). All the masses were taken using an electronic balance (Mettler Toledo AB204-S, Switzerland) with an uncertainty of

± 0.0001 g. Thus, the solid concentration of the sample solution of mole fraction, x, could be determined from eq 1.

$$x = \frac{(m_2 - m_0)/M_1}{(m_2 - m_0)/M_1 + (m_1 - m_2)/M_2} \quad (1)$$

where M_1 is the molar mole of drug and M_2 is the molar mass of the solvent.

At each temperature, the measurement was repeated three times and an average value is given in Table 1 along with uncertainty.

Table 1: Observed Mole Fraction Solubilities (*x*), Calculated Mole Fraction Solubilities (x_{ci}) and relative deviation (*RD*) of Cholesterol in some alcohols

T/K	$10^2 x$	$10^2 x_{ci}$	100 RD
Methanol			
293.15	0.04 ± 0.001	0.05 ± 0.002	1.8244
295.15	0.05 ± 0.004	0.05 ± 0.003	1.1317
298.15	0.06 ± 0.002	0.06 ± 0.003	-1.5861
300.15	0.06 ± 0.001	0.06 ± 0.005	-0.4226
303.15	0.07 ± 0.002	0.07 ± 0.003	0.8499
305.15	0.08 ± 0.002	0.07 ± 0.003	-1.6085
308.15	0.09 ± 0.004	0.08 ± 0.002	-1.4033
310.15	0.09 ± 0.001	0.09 ± 0.008	0.6753
313.15	0.10 ± 0.023	0.10 ± 0.002	0.6187
315.15	0.11 ± 0.018	0.11 ± 0.008	-0.3773
318.15	0.11 ± 0.048	0.12 ± 0.012	1.9646
Ethanol			
293.15	0.27 ± 0.023	0. 28 ± 0.030	0.2767
295.15	0.29 ± 0.035	0.29 ± 0.027	-0.2723
298.15	0.31 ± 0.018	0.31 ± 0.020	-0.2053
300.15	0.33 ± 0.017	0.32 ± 0.030	-0.4255
303.15	0.35 ± 0.020	0.34 ± 0.011	-0.3879
305.15	0.37 ± 0.011	0.36 ± 0.008	-0.7125
308.15	0.39 ± 0.017	0.38 ± 0.013	-0.2656
310.15	0.41 ± 0.020	0.40 ± 0.010	-0.5607
313.15	0.43 ± 0.028	0.43 ± 0.028	-0.2310
315.15	0.45 ± 0.013	0.45 ± 0.008	-0.2142
318.15	0.47 ± 0.023	0.48 ± 0.017	0.1852
Propanol			
293.15	0.98 ± 0.049	0.85 ± 0.037	-3.0371
295.15	1.03 ± 0.020	0.94 ± 0.024	-1.8753
298.15	1.09 ± 0.020	1.09 ± 0.020	0.0804
300.15	1.13 ± 0.026	1.20 ± 0.029	1.4010
303.15	1.18 ± 0.030	1.39 ± 0.030	3.7109
305.15	1.39 ± 0.017	1.54 ± 0.030	2.3800
308.15	1.69 ± 0.026	1.78 ± 0.037	1.2929
310.15	1.89 ± 0.032	1.96 ± 0.030	0.9157
313.15	2.19 ± 0.023	2.27 ± 0.044	0.9104
315.15	2.66 ± 0.014	2.50 ± 0.045	-1.6499

318.15	3.35 ± 0.020	2.90 ± 0.015	-4.2575
		Butanol	
293.15	1.39 ± 0.013	1.22 ± 0.037	-3.1028
295.15	1.45 ± 0.056	1.33 ± 0.030	-2.0309
298.15	1.52 ± 0.026	1.51 ± 0.032	-0.1273
300.15	1.58 ± 0.020	1.65 ± 0.023	1.0571
303.15	1.64 ± 0.021	1.87 ± 0.015	3.1808
305.15	1.89 ± 0.016	2.04 ± 0.024	1.8668
308.15	2.27 ± 0.030	2.31 ± 0.017	0.5441
310.15	2.51 ± 0.018	2.52 ± 0.012	0.0955
313.15	2.88 ± 0.011	2.87 ± 0.012	-0.1680
315.15	3.32 ± 0.015	3.12 ± 0.015	-1.8410
318.15	3.97 ± 0.026	3.55 ± 0.028	-3.5176

Results and Discussion

The mole fraction solubilities *x* of cholesterol in methanol, ethanol, propanol and butanol at from T = (293.15 to 318.15) K are summarized in Table 1. The variation of solubility with temperature is also shown in Figure 2. It is observed that solubility increases linearly with increase in temperature. Further, solubility is higher in butanol and a minimum in methanol. It means solubility increases as number of carbon increases. The solubility in these four alcohols can also be related to their dielectric constants and dipole moments [10] which are given in Table 2. It is known that increase is dielectric constant causes more solubility for polar or charged compounds, however in the present study; the reverse is observed. The dielectric constant of methanol is a maximum but in methanol less solubility was observed. The dipole moment of all the four alcohols is not much different.

Table 2: Dielectric constants and dipole moments of some alcohols

Solvents	Dielectric Constant	Dipole moment
Methanol	33.62	1.70
Ethanol	24.30	1.69
Propanol	20.33	1.657
Butanol	17.5	1.66

Further, the increase of chain length causes a decrease in acidity and polarity of molecules and an increase in basicity of hydroxyl oxygen. Cholesterol has ability for self-association and acts as proton donor in the association process with proton acceptors.[4] So, it readily associates with alcohol and association increases with increase in chain length. This association takes place mainly by hydrogen bonding.

Table 3: Constants A and B of equation 2, Absolute Average Deviation (AAD), and root Mean Square Deviation (rmsd) of Cholesterol in some alcohols

Solvents	*A*	*B*	10^5 rmsd	100 AAD
Methanol	-18.02	0.0357	0.003	0.15
Ethanol	-12.43	0.0223	0.005	-0.25
Propanol	-19.03	0.0487	3.113	-0.01
Butanol	-16.89	0.0426	3.149	-0.36

Table 4: Thermodynamic function of dissolution of cholesterol in some alcohols

Solvents	ΔG/kJ.mol^{-1}	-ΔH/kJ.mol^{-1}	-T ΔS/kJ.mol^{-1}
Methanol	18.10	12.81	5.25
Ethanol	14.20	6.49	7.70
Propanol	10.54	19.95	9.41
Butanol	9.80	17.38	7.58

Also, in alcohols, the growing number of carbon atoms causes a decrease in self association i.e., solvent-solvent interactions, which can be attributed to the presence of intermolecular hydrogen bonds. All these results in an increase in solubility of cholesterol in butanol.

Figure 2: Variation of mole fraction solubilities (*x*) and calculated mole fraction solubilities (x_{ci}) xith temperature for drug in different solvents. methanol; □, ethanol; ×, propanol; Δ and butanol; ○. x_{ci} is shown as dotted line for all the four solvents

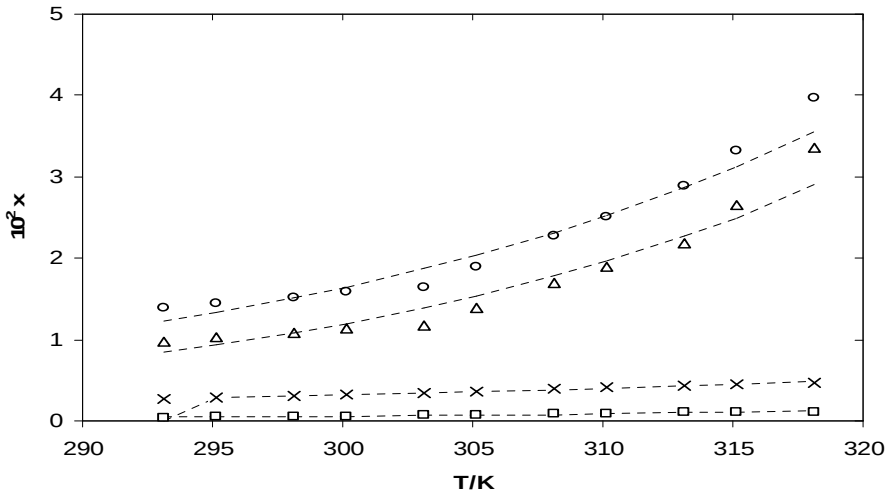


Figure 3: Solubility x of cholesterol as a function of temperature in methanol; □, ethanol; ×, propanol; Δ and butanol; ○.

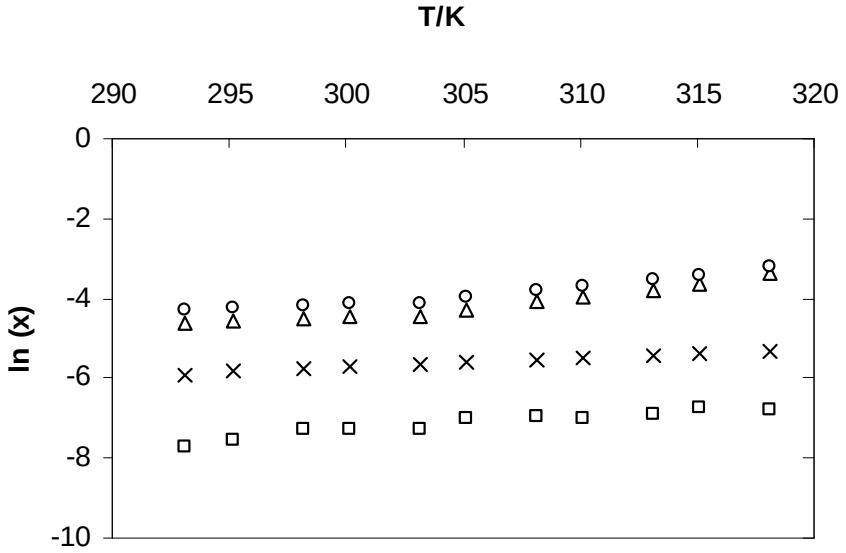
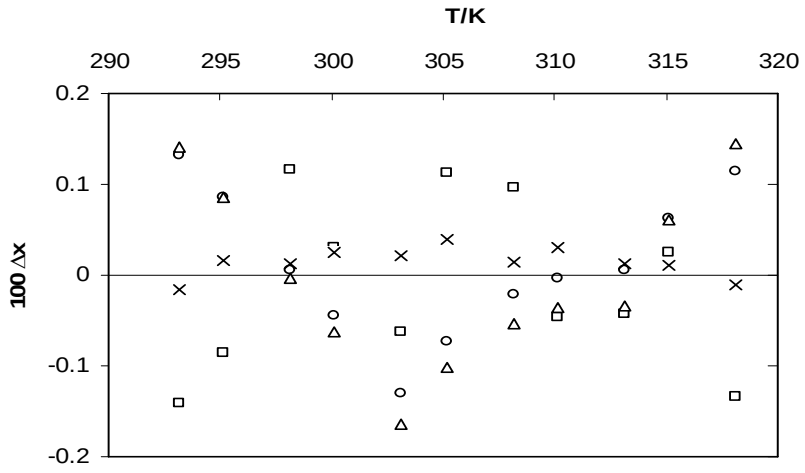


Figure 4: Fractional deviations Δx = x- x_c of cholesterol solubility at various temperatures in different solvents. methanol; □, ethanol; ×, propanol; Δ and butanol; ○.



As shown in Figure 2, the mole fraction solubility *x* of cholesterol was correlated as a function of temperature. The temperature dependence of cholesterol solubility in solvents is described by the modified Apelblat equation [11, 12]

$$\ln x = A + B\,(T/\mathrm{K}) \qquad (2)$$

where *x* is the mole fraction solubility of cholesterol; *T* is the absolute temperature and *A*, and *B* are the parameters in eq 2. The values of these parameters are given in Table 3. Further, the variation of ln x verses T is shown in Figure 3 which is found to be linear. The calculated solubilities x_{ci} are also reported in Table 1. The experimental solubility of drug in the studied

solvents was compared with calculated solubility (x_{ci}). The difference betxeen experimental and theoretical solubilities ($\Delta x = x - x_{ci}$) are plotted against temperature in Figure 4.

Further, absolute average deviations (AAD) and root-mean-square deviations (rmsd), calculated by equations 3 and 4 are listed in Table 3.

$$AAD = \frac{1}{N}\sum_{i}^{N} \frac{\chi_i - \chi_{ci}}{\chi_i} \quad (3)$$

$$rmsd = \left[\sum_{i=1}^{N} \frac{(\chi - \chi_{ci})^2}{N-1}\right]^{1/2} \quad (4)$$

where N is the number of experimental points and x_{ci} is the solubility calculated by eq. 2.

The relative deviations (RD) between the experimental and calculated values of solubilities are also calculated by equation 5 and are given in Tables 1.

$$Relative\ Deviation = \left(\frac{\chi - \chi_{ci}}{\chi_{ci}}\right) \quad (5)$$

The temperature dependence of log x was used to evaluate the molar enthalpy of solution, ΔH. Using the solubility data, the standard Gibbs energies of the dissolution process ΔG, were calculated using the following eq [13]

$$\Delta G = -RT \ln x \quad (6)$$

where x is the mole fraction of the investigated substance in the saturated solution.

Using ΔH and ΔG values, the standard entropies of solutions ΔS were obtained from the well known eq[14].

$$\Delta G = \Delta H - T\Delta S \quad (7)$$

These evaluated thermodynamic parameters are given in Table 4.

As evident from Table 4 that ΔG decreases as number of carbon atoms or CH_2 group increases. However, there is no regular trend for ΔH and TΔS values. For all the four alcohols, ΔH values are lower than those of TΔS suggesting thereby that the process of solvation is entropy dependent.

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