31.01% of Tenoxicam was retained in niosomes prepared using surfactant alone while niosomes prepared using surfactant - cholesterol mixtures retained 53.8% - 67.0% of the drug (Table I).

It appears from our preliminary studies that niosomes may be suitable carriers for local and oral therapy. By varying the vesicle composition, stable vesicles with optimum size range, entrapment efficiency and drug release properties can be prepared resulting in a formulation with optimum pharmacokinetic and therapeutic characteristics.

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Regression Analysis of Aqueous Solubility Data - Polycyclic aromatic hydrocarbons and Steroids

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The aqueous solubility data of polycyclic aromatic hydrocarbons and steroids was regressed to predict the level of solubility. Hildebrand - Scatchard equation format was used in the regression model. The correlations were fairly high (≈86%) for hydrocarbon series and appreciable for steroids (≈ 62%). A comparison of coefficients indicate that the solubility of steroids are twice that of the predictions obtained for polycyclic aromatic hydrocarbons. The functional groups on the skeleton structure might have interacted with water strongly and enhanced its solubility.

AQUEOUS solubility has long been identified as a key factor in the design of solution dosage forms. Water is generally recognised as a highly irregular solvent, and therefore, aqueous solution do not comply with regular solution theory.[1] However, if the solute is sufficiently nonpolar or inert, the aque-

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ous solution would become dilute. The solute - solvent interactions are weaker in dilute solutions and thus may approach regular solutions behaviour. It is assumed here that the limitations imposed by water are uniform, at least, for a homologous series and, therefore, are considered to be constant.

The present communication has made an attempt to fit the aqueous solubility data into Hildebrand - Scatchard equation.[2] Two structurally related chemical categories namely polycyclic aromatic hydrocarbons and steroids were selected for the regression analysis. They are lipophilic and contain rigid molecules.

Such an analysis allow us to describe the extent of deviation from the regular solution theory.

The solubility of a solute in nonpolar or moderately polar solvents is described by the Hildebrand - Scatchard equation.[2] The mole fraction solubility (X_2) of a solute is estimated using the equation

$$-\log x_2 = -\log X_2^i + \frac{\phi^2 V_2}{2.303RT}(\delta_1 - \delta_2)^2 \quad \ldots\ldots (1)$$

Where X^i_2 is ideal mole fraction solubility; V_2 is molar volume of solute; ϕ_1 is the volume fraction of solvent; R is ideal gas constant; T is the working temperature (298°); and δ_1 and δ_2 are the solubility parameters of solvent and solute, respectively. The equation (2) was proposed for rigid molecules to predict ideal solubility based on entropy fusion approximation.[3]

$$\log X^1_2 \approx 0.01\ (mp - 25) \quad \ldots\ldots\ldots\ldots (2)$$

In equation (2), mp is the only variable. In general, for dilute solutions the volume fraction, ϕ_1, is approximated to unity. Solubility parameter of water is 23.4 H. Thus the second term can be approximated to the equation (3) by substituting the appropriate constants.

$$0.0007333V_2\ (23.4 - \delta_2)^2 \quad \ldots\ldots\ldots\ldots (3)$$

For poorly soluble compounds, the molar solubility (S_w) is simply the mole fraction solubility (X_2) multiplied by 55.5 (the molarity of water) so that[3]

$$\log S_w = \log X_2 + 1.74 \quad \ldots\ldots\ldots\ldots (4)$$

Substitution of the terms obtained in equations (2) and (3) into equation (1) and converting the X_2 into S_w (equation 4), the following equation can be obtained.

$$\log S_w = -0.01\ (mp - 25) + 0.000733\ V_2 (23.4 - \delta_2)^2 - 1.74 \quad \ldots\ldots\ldots\ldots (5)$$

The regression analysis was attempted in the format of equation (5).

The solubility parameter and molar volume of the compounds under study were estimated using the software developed by us based on Fedors fragmental constants.[4] The melting point and the aqueous solubility data was extracted from earlier reports.[3] Multiple regression analysis was performed using Lotus 1-2-3 (3.0) package on a PC/AT (Quickfox).

Polycyclic Aromatic Hydrocarbons

The aqueous solubility data was processed for multiple regression analysis in the pattern of Equation (5). The equation is

$$\log S_w = -0.018\ (mp-25) - 0.0001\ V_2 (23.4 - \delta_2)^2 - 1.41028 \quad \ldots\ldots (6)$$

$n = 32$; $s = 0.6485$; $R^2 = 0.8606$

The R^2 value (0.86) indicated fairly high degree of correlations. The coefficient of mp was - 0.018, which was lower than the expected value of - 0.01 (cf. equation 5). The coefficient of the second term in right - side of the equation (6) was 0.0001, which was less than the expected value (0.0007). The sign of the coefficient in equation 6 was negative, while in equation 5 it was positive. Conceptually, molar volume is expected to have endoergic relationship

with the aqueous solubility.[5] Similar observations were obtained when solvatochromic parameters were correlated with the aqueous solubility[6]. The constant is nearly same as expected in the equation(5). The aqueous solubility of these compounds were much lower than those expected by equation 5.

Steroids

The regression equation for the experimental aqueous solubility data is

$$\log Sw = - 0.006 (mp-25) - 0.00005 V_2 (23.4 - \delta_2)^2 - 0.8146 \quad (7)$$

$n = 19$; $s = 0.3668$; $r^2 = 0.6263$.

The correlation coefficient is low (0.6263). The coefficients are less than those expected (equation 5). The accuracy of equation (7) is ≈62%. The values were comparable to the observed solubility. The coefficients and the constant in equation (7) were about half of that were obtained in Polycyclic aromatic hydrocarbons (equation 6). This trend indicates that the aqueous solubility of steroids might be twice that of the predicted values in polycyclic aromatic hydrocarbons. This may be possible through the specific interaction (hydrogen bonding) of the functional groups with water. While discussing about the solubility of steroids, it was mentioned that strongly hydrophilic substituents on the skeleton was desirable to achieve appreciable aqueous solubility.[1] These observations are in tune with the present analysis.

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