

Intermolecular Interactions in Ternary Solutions of B₆ Vitamin

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The spectral shifts in the UV electronic absorption spectra of B₆ in protic solvents were correlated with the macroscopic parameters (refractive index and electric permittivity) of solvent mixtures. By means of multiparameter regression coefficients technique, the contributions of the intermolecular interactions upon the spectral shifts as a function of the solvent macroscopic parameters were expressed. Relative to the solutions studied, the dependence of the wave number in maximum electronic band of B₆ vitamin on the solvent macroscopic parameters demonstrates in fact the prevalence of the orientation. Through Spartan (software) program, some electrical parameters and global descriptors of B6 vitamin were computed.

Keywords: solvents effect, absorption spectra, B₆ vitamin

In the first part of the introduction we will try a familiarity with terms and concepts used in this paper. In the well-known chemical terms, the protic solvent is a solvent that has a hydrogen atom bound to an oxygen (as in a hydroxyl group) or a nitrogen (as in an amine group). Mutually, any solvent that contains labile H⁺ is named a protic solvent.

In the pharmaceutical nomenclature, B₆ vitamin (also known as pyridoxine) is part of B group vitamin and is a water-soluble vitamin. At the same time, this vitamin is an organic compound with molecular formula C₈H₁₁NO₃. The core of the B₆ vitamin contains a pyridine ring which is attached to the hydroxyl and methyl groups. It is involved in the process of making serotonin and contributes to normal functioning of the nervous system, to formation of red blood cells, to the normal function of the immune system.

Studies on the electronic absorption spectra of some biologically active molecules in solutions allowed obtaining some information about the physico-chemical properties of the investigated molecules, or determining the nature of interactions between the molecules of the solvent but also, obtaining information about the transition types responsible for obtaining electronic absorption bands. This study aims to analyze the influence of some polar protic solvents on the electronic absorption spectra of B6 vitamin in the UV-Vis range to obtain information relating to the nature of the intermolecular interactions solute-solvent. At the base of this study there are a number of theoretical models and experimental methods that examine the interaction of light with the substance. There were developed several studies regarding the influence of solvents on the electronic absorption spectra of organic molecules in both binary and ternary solutions. Any solution requires interaction between the solute and solvent molecules.

To investigate a solution using spectroscopy means we assume the use of the spectrally active molecules as "sounders" in very small concentration in a pure solvent which gives information about the local reactive electric field from liquid solution by the spectral changes. Solvation of organic molecules in different solvents affects the electronic absorption spectra due to interactions between the solute-solvent molecules. These interactions acting in

solutions induce spectral shifts or modifications in the shape and band intensity.

Structure and interactions between molecules are difficult to obtain experimentally but using molecular modelling programs there can be obtained physico-chemical properties of the molecules but also information about the interactions that take place in different solvents.

In our present paper, the main program used for this purpose is called Spartan. In a general way, it is a molecular modeling and computational chemistry application from Wavefunction [1]. Structurally this software contains codes for semi-empirical methods, *ab initio* models, density functional models, post-Hartree-Fock models, molecular mechanics and thermochemical recipes.

In this way, using the molecular programs based on some mathematical approaches of molecular MO there can be obtained the most likely structure of the molecule after optimization geometry of molecules.

Determination of the structural formula of organic molecule is very important for drugs because in order to be biologically active, they need to fix on other molecules. In the present study the methods of investigation based on the spectral analysis of UV-VIS range allowed the obtaining of information concerning the nature of intermolecular interactions in ternary solutions. The spectral shifts were correlated with macroscopic parameters of the solvent such as electric permittivity and refractive index. Solvent theories developed by some authors [2-10] are related to intermolecular interactions that occur in the solutions of organic compounds. The universal and specific interactions will be taken into account in the frequency shift expression.

Attempts to evidence some empirical relations between the spectral characteristics and macroscopic parameters of the solvent were made in the first stage of the research on the intermolecular interactions. Intermolecular interactions were described in some kinetic or cell models [11-16]. These models based on statistical [17-23] and dielectrical [24] approach neglected the specific interactions. In order to take them into account, a supplementary term has been added to those resulting from theoretical treatment [25-27].

On the basis of the relations established by different models, there can be estimated the contribution of each

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type of interaction between the spectrally active molecule and the solvent molecules. Usually, the supply of the specific interactions is expressed by semi-empirical terms dependent on the local distribution of the electronic charges in the interacting molecules [28].

Experimental part

In Bakhshiev theory [17], the total shift measured in the electronic absorption spectra is expressed by relation of type (1):

$$\tilde{\nu} = \tilde{\nu}_0 + C_1 \cdot f(\epsilon) + C_2 \cdot f(n) \quad (1)$$

In relation (1) $\tilde{\nu}(\text{cm}^{-1})$ is the wave number in the maximum electronic absorption band, $\tilde{\nu}_0(\text{cm}^{-1})$ has the significance of the wave number in the maximum electronic absorption band recorded for the gaseous phase

of the spectrally active molecule, $f(\epsilon) = \frac{\epsilon - 1}{\epsilon + 2}$ and

$f(n) = \frac{n^2 - 1}{n^2 + 2}$ are the solvent functions which depend on

the electric permittivity or refractive index. The $f(\epsilon)$ function expresses the contributions of the orientation interaction to the total spectral shift and $f(n)$ expresses the contributions of dispersive-induction-polarization interactions to the spectral shift.

Taking into account the specific interactions, a supplementary term must be added to equation (1), one obtaining relation (2):

$$\tilde{\nu} = \tilde{\nu}_0 + C_1 \cdot f(\epsilon) + C_2 \cdot f(n) + \Delta\tilde{\nu}_{\text{sp.int. er.}} \quad (2)$$

In equations (1-2) the regression coefficients C_j , $j=1, 2, 3..$, depend on some microscopic parameters such as dipole moments or polarizabilities of the interacting molecules. The separation of the universal and specific interactions permits to estimate the strength of each type of interactions acting in the solution. A great value of the regression coefficient shows that the interaction expressed by this parameter is dominant in the spectral shift [29]. The current statistical methods allow the estimation of the degree of correlation of a large number of experimental data.

Using the molecular program [30] there may be obtained the values of some parameters for ternary solutions such as dipole moment, polarizability, total energy, molecular orbital HOMO, LUMO energies and some global descriptors- electronegativity, hardness, chemical potential, electrophilicity index.

According to Koopman's theory, the frontier orbital energies are given by [31]:

$$\begin{aligned} I &= -E_{\text{HOMO}} \\ A &= -E_{\text{LUMO}} \end{aligned} \quad (3)$$

The concept of absolute electronegativity and absolute hardness are defined by [23-26]:

$$\begin{aligned} \chi &= \frac{I + A}{2} \\ \eta &= \frac{I - A}{2} \end{aligned} \quad (4)$$

The chemical potential is related to the free energy corresponding to one molecule when it is into condensed state:

$$\mu = \frac{E_{\text{HOMO}} + E_{\text{LUMO}}}{2} \quad (5)$$

Electrophilicity index is considered as a measure of stabilization in energy when the system acquires an additional electronic charge [32]:

$$\omega = \frac{\mu^2}{2\eta} \quad (6)$$

These molecular properties are correlated with the reactivity and biological activity of B_6 vitamin. B_6 vitamin was provided from Sigma Aldrich Co. Polar solvents (ethanol and water) are used for analysis of electronic absorption spectrum of B_6 vitamin in ternary solutions belonging to the category of protic solvents and plays an important role in the formation of the hydrogen bond with this vitamin. For different volumetric ratios 100: 0, 90: 10, 80: 20, 70: 30, 60: 40, 50: 50, 60: 40, 70: 30, 20: 80, 10: 90, 0: 100, there have been calculated the functions $f(\epsilon)$ which highlight the orientation-induction interactions, $f(n)$ which highlights the dispersive interactions and the function $f(n, \epsilon)$ for universal interactions, the strong dependences of the wave numbers in the maximum of the electronic absorption band on these functions in UV range were obtained.

The refractive index of the solvents was measured at room temperature at $\lambda = 589.2 \text{ nm}$ with an Abe refractometer and electric permittivity was approximated by using formula:

$$\epsilon_{\text{mix}} = \frac{\epsilon_1 \cdot x_1 + \epsilon_2 \cdot x_2}{100} \quad (7)$$

where x_1, x_2 and ϵ_1, ϵ_2 are the volumetric fraction of the solvents in the ternary solutions, dielectric constants, respectively.

Results and discussions

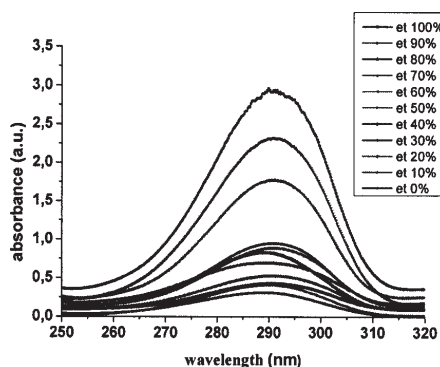


Fig. 1. Electronic absorption spectra of B_6 vitamin in ethanol-water mixtures

The electronic spectra of ternary solutions were recorded with a Shimadzu 1700 UV spectrophotometer with a data acquisition system.

Electronic absorption spectra of B_6 vitamin in ethanol-water mixture is shown in figure 1.

The volumetric fractions of the protic solvents and the wave number in the ICT of UV electronic band in ternary solutions B_6 + ethanol + water are given in table 1.

For the ternary solution formed by B_6 -ethanol-water it is found that, as the ethanol concentration increases there is a shifting of the electronic absorption spectrum to small wavelengths (hipsocrom effect) as shown in figure 2 (a).

Analyzing electronic absorption spectra in ternary solution formed of B_6 -ethanol-water and dependence between the wave number in the maximum electronic absorption band, $\tilde{\nu}_0(\text{cm}^{-1})$ and $f(\epsilon)$, $f(n)$, $f(n, \epsilon)$ functions, there is found that the polarization-dispersive-induction and

Nr. Crt.	Ethanol (%)	n	$\epsilon_{\text{mixture}}$	$f(n) = \frac{n^2-1}{n^2+2}$	$f(\epsilon) = \frac{\epsilon-1}{\epsilon+2}$	$f(\epsilon, n) = \frac{\epsilon-1}{\epsilon+2} \cdot \frac{n^2-1}{n^2+2}$	$\tilde{\nu}$ (cm ⁻¹)
1	100	1.3618	24.5	0.2216	0.8867	0.6651	34530
2	90	1.3628	30.06	0.2222	0.9064	0.6842	34507
3	80	1.3627	35.62	0.2221	0.9202	0.6981	34507
4	70	1.3615	41.18	0.2215	0.9305	0.7090	34483
5	60	1.3595	46.76	0.2204	0.9384	0.7180	34452
6	50	1.357	52.30	0.2190	0.9447	0.7257	34426
7	40	1.349	57.86	0.2146	0.9498	0.7352	34388
8	30	1.347	63.42	0.2135	0.9541	0.7406	34364
9	20	1.343	68.98	0.2112	0.9577	0.7465	34356
10	10	1.336	74.54	0.2073	0.9608	0.7535	34341
11	0	1.332	80.1	0.2051	0.9634	0.7583	34317

Table 1
PHYSICAL PARAMETERS OF THE SOLVENTS AND WAVE NUMBERS IN THE MAXIMUM OF UV BAND FOR TERNARY SOLUTIONS OF B₆ VITAMIN

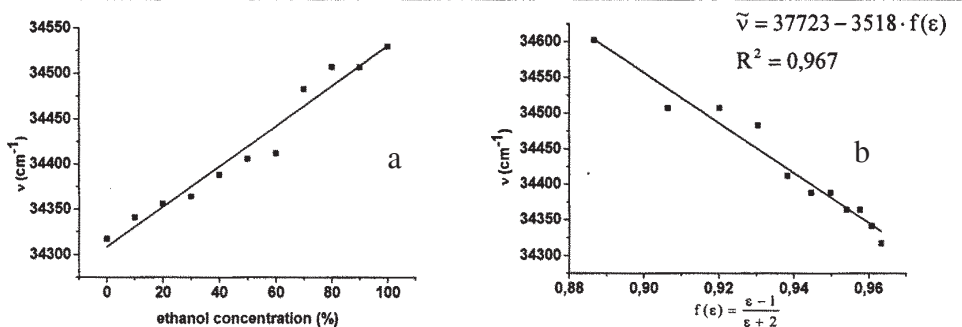


Fig. 2. Linear correlations between $\tilde{\nu}$ and ethanol concentrations (a), and

$$f(\epsilon) = \frac{\epsilon-1}{\epsilon+2}, (b)$$

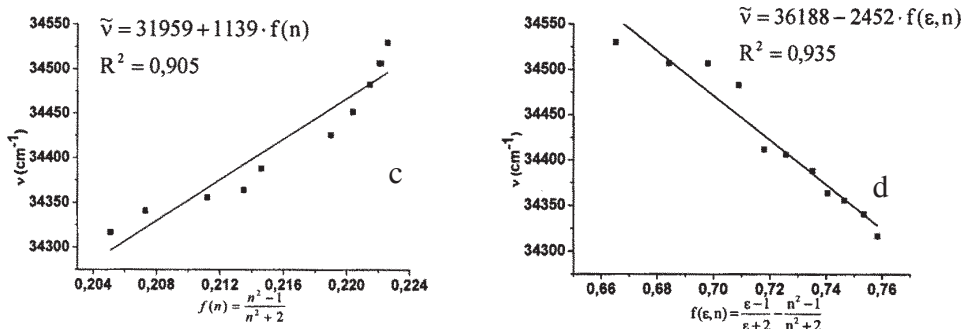


Fig. 3. Linear correlations between $\tilde{\nu}$

and $\tilde{\nu}$ and $f(n) = \frac{n^2-1}{n^2+2}$ (a), and

$$f(\epsilon, n) = \frac{\epsilon-1}{\epsilon+2} \cdot \frac{n^2-1}{n^2+2} (b)$$

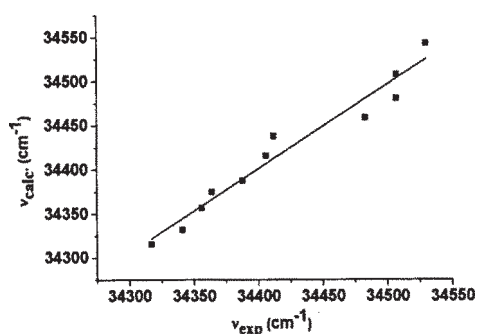


Fig. 4. Linear dependence between $\tilde{\nu}_{\text{calc.}} = f(\tilde{\nu}_{\text{exp}})$

$$\tilde{\nu}_{\text{calc.}} = 35170 + 4837.74 \cdot f(\epsilon) - 1916.05 \cdot f(n) + 1502.74 \cdot \delta(\text{ppm}) \quad (8)$$

The values of the different interactions in ternary solutions of vitamin B₆ can be estimated and compared with each other according to the results of the table 2.

Table 2
CONTRIBUTION AS A PERCENTAGE OF THE INTERACTIONS IN TERNARY MIXTURE

Type of interaction	UV
$C_1 \cdot f(\epsilon)$	41.34%
$C_2 \cdot f(n)$	24.07%
$C_3 \cdot \delta(\text{ppm})$	34.58%

universal interactions are present. Linear correlations that are obtained from the charts in figures 2(b), 3(a-b) confirmed the coexistence of these interactions.

The contribution of specific interactions to the total spectral shifts was approximated by the distance from the first bisecting and the line which contains the points of ($\tilde{\nu}_{\text{calc.}}, \tilde{\nu}_{\text{exp.}}$) plane (fig. 4).

For ternary solution B₆-ethanol-water, the empirical equation which describes the different interactions to the total spectral shift is given by the equation (8):

The positive value of C_1 coefficient suggests that orientation forces cause a spectral shift towards lower wavelengths; C_2 has a negative value meaning that the universal interactions cause a shift towards high wavelengths.

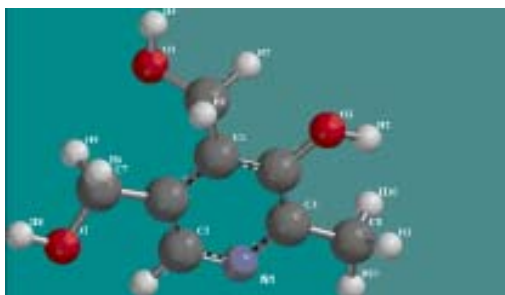


Fig. 5. Optimized geometry of B₆ vitamin

Table 3

COMPUTED VALUES OF SOME ELECTRICAL PROPERTIES AND GLOBAL DESCRIPTORS FOR B₆ IN GROUND STATE

No.	Property	B ₆
1.	Dipole moment (Debye)	2.73
2.	Polarizability (a.u.)	52.869
3.	E _{HOMO} (eV)	-9.206
4.	E _{LUMO} (eV)	-0.231
5.	Energy gap (ΔE) (eV)	8.975
6.	Electronegativity (eV)	4.4875
7.	Hardness (eV)	4.7185
8.	Chemical potential (eV)	-4.4875
9.	Index of electrophilicity (eV)	2.4806

Table 4

GLOBAL DESCRIPTORS FOR TERNARY SOLUTIONS OF B₆

No.	Property	B ₆ +w+et
1.	Dipole moment (Debye)	2,17
2.	Polarizability (a.u.)	58,935
3.	E _{HOMO} (eV)	-9,333
4.	E _{LUMO} (eV)	-0,270
5.	Energy gap (ΔE) (eV)	9,603
6.	Electronegativity (eV)	4,801
7.	Hardness (eV)	4,531
8.	Chemical potential (eV)	-4,801
9.	Index of electrophilicity (eV)	2,543

Using the Koopman's theorem one can characterize the chemical potential (μ), defined by the relationship (i. 46) as the tendency of a system in equilibrium of losing electronic density, being equal with another chemical concept of extreme importance, the electronegativity (χ) (eq. 5) taken with the sign reversed. Strength (hardness, η) defined by equation (4) is a quantity that characterizes the resistance of a system for the transfer of the task, being correlated directly with the chemical stability of a molecule, while softness (S) is a system's polarizability.

Electrophilicity index (ω) specified by the equation (6) is defined as the change in energy system when a reagent is put in contact with a nucleophil perfect (i.e. a mass of electrons with the chemical potential and zero hardness) and describes the ability of a molecule to accept electronic density. Thus, we can say that a good electrophil is a molecule with a reduced amount for both μ and η .

Table 5
GLOBAL DESCRIPTORS FOR BINARY SOLUTIONS OF B₆

No.	Molecular complex	χ (eV)	η (eV)	μ (eV)	ω (eV)
1.	B ₆ +water	5.195	4.471	-5.195	3.018
2.	B ₆ + ethanol	5.062	4.456	-5.062	2.875

The chemical reactivity and the stability of the system (ternary solutions) were compared with those from binary solutions (B₃+water and B₃+ethanol) tabulated in tables 4 and 5.

Higher reactivity is demonstrated by the hardness as seen from the values contained in tables 4 and 5. In accordance with the principle of maximum hardness which postulates that the system is more reactive as the hardness is lower, it can be observed that the molecular structure from ternary solutions is more reactive than binary solutions. Comparing values of (hardness) η parameter for binary and ternary solutions of B₆ we can assert that the ternary is more reactive than binary solutions (lower hardness).

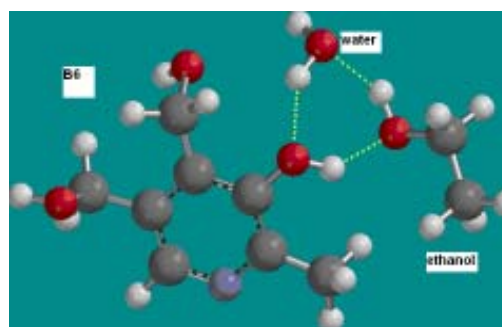


Fig. 6. Possible intermolecular hydrogen bonds formed between B₆-water-ethanol (red-oxygen atoms, gray-carbon atoms, white-hydrogen atoms, blue-nitrogen atom, broken yellow line-hydrogen bonds)

Because the electrophilicity index is considered a measure of the stability of the system, we can say that the ternary solution is more stable than the binary solutions.

Between vitamin B₆ and ethanol-water mixture can form hydrogen bonds as shown in figure 6.

The electrostatic potential is the energy of interaction of a point positive charge (an electrophil) with the nuclei and electrons of a molecule. Negative electrostatic potentials (fig. 9) indicate areas that are prone to electrophilic attack. Colours towards red indicate negative values of the electrostatic potential, while colours towards blue indicate positive values of the potential.

The surface colour reflects the magnitude and polarity of the electrostatic potential. Gray, violet and blue colours correspond to a negative electrostatic potential - regions of the molecule susceptible to electrophilic attack.

The HOMO and LUMO orbitals were found to be useful to explaining chemical reactivity. Electrophilic attacks were shown to correlate very well with atomic sites having high density of the HOMO orbital, whereas nucleophilic attacks correlated with atomic sites having high density of the LUMO orbital (fig. 8).

By convention, the colour blue indicates a high concentration of orbitals, while the colors to red indicate a low concentration. LUMO orbitals map shows the potential areas where nucleophilic attack will occur. In the case of carbon atoms an electrophilicity characteristic is

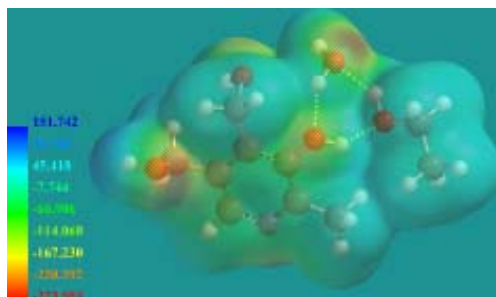


Fig. 7. Electrostatic potential map for ternary solutions of B₆

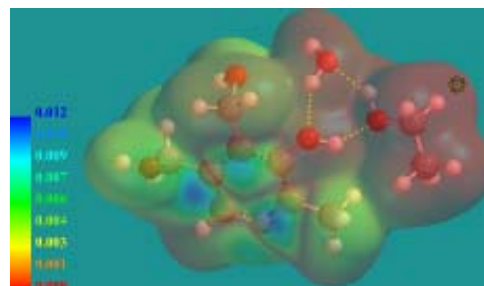


Fig. 8. LUMO map for ternary solutions of B₆

observed. The intense red region shows where there will be most likely the nucleophilic attack.

The almost classical aspects presented in the paper are interesting in conjunction with the major themes of contemporary chemistry and physics. In present, the assimilation of the B6 vitamin copolymeric compounds in medicine and cosmetics must fulfill the complexity of the biological issues that result from using them.

We note that the B6 vitamin can be incorporated in the polymeric structures to improve its functions. In a few words, it is important to embed B6 vitamin in copolymers in order to improve product quality cosmetics and pharmaceutical industry.

The formation of copolymers allows their transport from the cis zone through membrane and the compound action in the trans zone, sometimes inaccessible to a simple vitamin in its classical form. In accordance with the first author [33-35], in theory, it is easy to handle today the polymers of different lengths through nanometric pore membrane.

Conclusions

In the ternary mixture analysed it was found that as the concentration of the solution increases, there is a shifting of the spectrum to small wavelengths, interpreted as Hypsochromic shift or effect.

In quantitative terms, the computational procedures showed that the ternary solutions are less polar (lower dipole moment), because hydrogen bonds stabilize the fundamental state better than the excited state.

The calculation of the global descriptors (here, the hardness parameter values) has shown that the ternary solutions are more reactive than the binary solutions.

Thanks to these results, we can say that the ternary solution is more stable than the binary solution. This aspect is attributed to the fact that the electrophilicity index is considered a measure of the system's stability.

A realistic pseudo 3D image, figure 5, related to the optimized geometry of vitamin B6 is presented.

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