PECULIARITIES OF CAFFEINE AND CAFFEINE SODIUM BENZOATE AQUEOUS SOLUTION IN PRESENCE OF FULLERENE C_{60}

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Abstract. Aromatic ligands behavior (caffeine and caffeine sodium benzoate) was analyzed in pure aquatic solution and in presence of fullerene C_{60}. To investigate the influence of fullerene C_{60} conductomertric titrational curves were obtained. Presence of interaction was confirmed by difference of conductivities of C_{60}/ligand mixture and total conductivities of pure C_{60} and pure ligand solutions at the same concentrations used in mixture. Significant influence was noticeable with the caffeine salt. The complexation caused noticeable reduction of ligand dissociation and as a result lowering the conductivity of solution. The results of this work can find application in improving the ways of drug delivery by means of their longer preservation in their native form.
Key words: *caffeine, caffeine sodium benzoate, C_{60} fullerene, molecular aggregation, aquatic solutions.*

INTRODUCTION

One of the most common methods of treatment is the combinative drugs therapy, manifested in reduction of drugs negative effects or varying its physicochemical properties: solubility, affinity, etc. In this regard, it is extremely important to identify the nature of the mechanisms of drugs complex behavior

Despite the large amount of information, there are still disputes over the nature of fullerene and ligands complexation in aquatic solution [1-3].

The aim of the research was to perform the evidence of fullerene C_{60} impact on the properties aromatic molecules (by example of caffeine and caffeine sodium benzoate).

Caffeine sodium benzoate was chosen as the target of the study because small conductivity values of pure caffeine aquatic solutions.

EXPERIMENTAL PART

Fullerene C_{60} was produced by Kratschmer's technique [4]. The water solution of fullerene C_{60} was obtained firstly by means of dissolving fullerene in toluene. Second stage was dissolving toluene with the fullerene in water followed by evaporation of the extract in a rotary vacuum evaporator under reduced pressure. [5] Concentration of fullerene C_{60} was 0.1 mmol.

Conductometric measurements of all the solutions were performed at 23 ^{o}C with conductivity portable meter ProfiLine Cond 3110 with a TetraCon cell:

- conductivity range 0.0...1000 mS/cm ± 0.5 % of measured value;
- salinity range 0.0...70.0 (as per IOT).

The purity of all the compounds was verified with fourier transform infrared spectrometer FT-801, Simex, equipped with "cat's eye" optical scheme based on ZnSe beamsplitter. Spectral range 470-5700 cm^{-1}. All IR spectra were obtained via resolution 4 cm^{-1}, 10 scans per specter, using disturbed total internal reflection (DTIR) module with a ZnSe flange. Spectra processing was handled in ZAIR 3.5 software package.

RESULTS AND DISCUSSION

In the framework of conductometric titration the electrical conductivity σ was measured at various concentrations for aqueous solutions of compounds. The results are shown in Table 1.

Table 1. Values of conductivity (**σ**) and specific conductivity (**σ_{sp}**) based on concentration (**C**) of caffeine and caffeine sodium benzoate at 23 °C in aquatic enviroment

Caffeine			Caffeine sodium benzoate		
C, mmol	σ, mcS/cm	σ_{sp}, mcSm/(cm* mmol)	C, mmol	σ, mcS/cm	σ_{sp}, mcS/(cm* mmol)
0,16	3	18,7	0,1	38,4	384
0,2	3,3	16,5	0,2	41,7	208,5
0,3	3,6	12	0,3	52	173,3
0,4	3,6	9	0,4	58,5	146,2
0,5	3,6	7,2	0,5	66,7	133,4
0,6	3,5	5,8	0,6	70,3	117,1
0,7	3,5	5	0,7	88,2	126
0,85	3,4	4	0,84	95	113
0,9	2,9	3,2	0,9	106,6	118,4
1,27	2,8	2,2	1	120	120
1,5	2,5	1,6	1,3	147	113
1,7	2,6	1,5	2	221	110,5
4	2,7	0,6	2,6	288	110,7
6	2,9	0,5	4	425	106,2
8	3,2	0,4	6	631	105,2
10	3,2	0,3	8	841	105,1
12	3,2	0,26	10	1042	103,7
14	3,3	0,23	12	1245	104
16	3,3	0,2	14	1457	102,2
18	3,6	0,2	16	1635	101,3
20	3,9	0,1	18	1824	101,1
-	-	-	20	1998	99,9

While increasing the general conductivity with the ligand concentration rising in both solution (caffeine and caffeine sodium benzoate) the specific (**σ_{sp}**) conductivity was reducing (fig. 1).

$$\sigma_{sp} = \frac{\sigma}{C}. \quad (1)$$

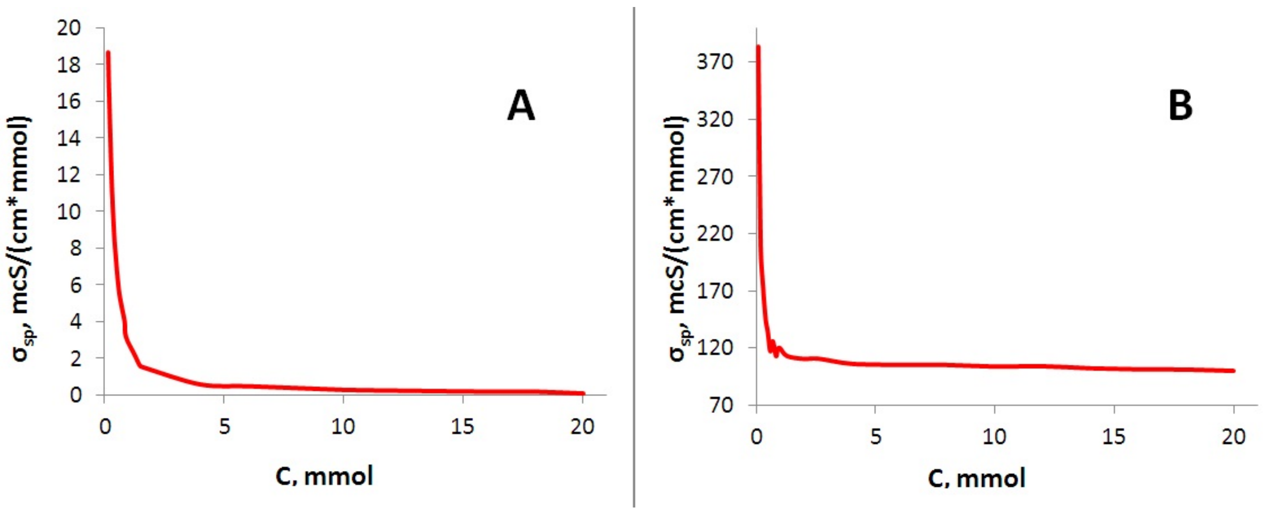

Figure 1. Dependences of specific conductivities of caffeine (**A**) and caffeine sodium benzoate (**B**) aquatic solutions on concentration of the compounds

Table 2. Values of conductivity (**σ**) based on concentration (**C**) of pure caffeine at 23 °C and in mixture with fullerene C_{60} in aquatic enviroment

C_{60}		Caffeine		Caffeine + C_{60}	
C, mmol	σ, mcS/cm	C, mmol	σ, mcS/cm	C, mmol	σ, mcS/cm
0,01	2,9	0,16	3	0,16	4,2
		0,4	3,6	0,4	4,5
		0,7	3,5	0,7	4,9

Table 3. Values of conductivity (**σ**) based on concentration (**C**) of pure caffeine sodium benzoate at 23 °C and in mixture with fullerene C_{60} in aquatic enviroment

C_{60}		Caffeine sodium benzoate		Caffeine sodium benzoate + C_{60}	
C, mmol	σ, mcS/cm	C, mmol	σ, mcS/cm	C, mmol	σ, mcS/cm
0,01	2,9	0,1	38,4	0,1	38,1
		0,4	58,5	0,4	48,3
		0,7	88,2	0,7	85,4

Such not linear dependences of conductivity on concentration point the selfassociation processes presence.

The next step was to measure the conductivities of pure fullerene C_{60} solution and of the mixtures of fullerene with each drug avoiding ligands concentration changes (tables 2, 3).

Based on the dependencies (fig. 2), we can conclude that the conductivity of the solution containing fullerene C_{60} mixture with each of the ligands is less than the total conductivity of pure solutions of fullerene and ligands at the same concentrations as in the mixture:

$$\sigma_{mix} < \sigma_{C_{60}} + \sigma_l, \tag{2}$$

where σ_{mix} – conductivity of fullerene C_{60} and ligand solution; $\sigma_{C_{60}}$ – conductivity of fullerene C_{60} solution; σ_l – conductivity of pure ligand solution.

In case of caffeine sodium benzoate the conductivity of mixture was even less than the conductivity of pure ligand solution. This fact clearly demonstrates stabilizing effect of fullerene C_{60} on caffene salts. It results in dacresing dissociation constant and consequently conductivity.

Caffeine does not dissociate into ions and the values of conductivity for it turned out to be relatively small. Based on this, it was concluded that the change in conductivity are caused by the interaction of caffeine with a solvent. Therefore the presence of fullerene C_{60} effects in lowering of caffeine SASA (solvent accessible surface area) resulting in lowering of conductivity in general.

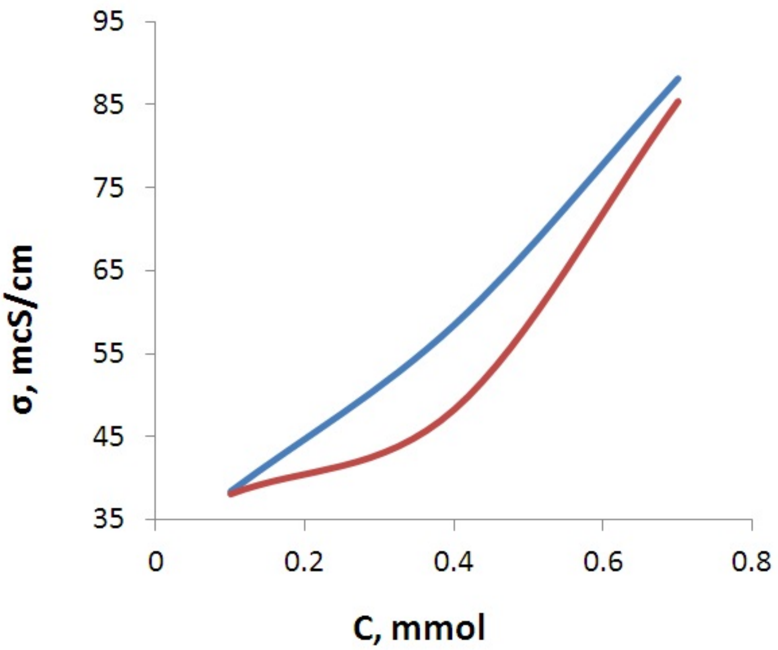

Figure 2. Dependences of conductivity of pure caffeine sodium benzoate aquatic solution (**blue**) and its mixture with the fullerene C_{60} (**red**) on concentration of the compounds

CONCLUSION

The evidence of heteroassociation between the compounds can be testified based on the comparison of the conductivity values of pure aromatic ligands solution and its mixture with the fullerene C_{60}. Insignificant concentration of fullerene C_{60} causes perceptible changes in behavior of aromatic ligands prone to dissociate into ions (caffeine sodium benzoate). These features could be applied in improvement of drugs delivery methods, by means of keeping their native structure for longer period excluding the use of shells and capsules. Preservation of active components in such way may result in dose reduction and side effects decrease.

References:

1. Evstigneev M.P., Lantushenko A.O., Golovchenko I.V. Hidden entropic contribution in the thermodynamics of molecular complexation. *PCCP: Physical Chemistry Chemical Physics*, 2016, vol. 18, no. 11, pp. 7617-7625.
2. Evstigneev V.P., Pashkova I.S., Kostjukov V.V., Evstigneev M.P., Hernandez Santiago, A.A. Optimal experiment design: link between the concentration and the accuracy of estimation of aggregation parameters. *Chemical Physics Letters*, 2016, vol. 664, pp. 133-137.
3. Borowik A., Prylutskyy Y., Kawelski Ł., Kyzyma O., Bulavin L., Ivankov O., Cherepanov V., Wyrzykowski D., Kaźmierkiewicz R., Gołuński G., Woziwodzka A., Evstigneev M., Ritter U., Piosik J. Does C_{60} fullerene act as a transporter of small aromatic molecules? *Colloids and Surfaces B: Biointerfaces*, 2018, vol. 164, pp. 134-143.
4. Kratschmer, W., Lamp, L.D., Fotiropoulos, K., Huffman, D.R. Solid C_{60} – a new form of carbon. *Nature*, 1990, vol. 347, no. 9, pp. 354-358.
5. Serdyuk I.E., Belochkina I.V., Kryshtal A.P, Roshal A.D., Nekludov I.M., Borts B.V., Voevodin V.N., Tkachenko V.I., Sandomirskyy B.P. Preparation and biological activity of aqueous colloid solutions of C_{60} and C_{70} fullerene mixtures. *Biotechnologia Acta*, 2011, vol. 4, no. 5, pp. 64-70.