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Study of gallic acid antioxidant molecule in interaction with solvents, aiming its utilization as stabilizer of magnetic nanoparticles in suspensions

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I. INTRODUCTION

Oxidative stress, i.e. free radicals overproduction and accumulation, may cause various diseases in human population. The gallic acid, a natural and simple polyphenol has strong antioxidant activity by its action of scavenging the free radicals, namely the reactive oxygen species (ROS) (Badhani et al., 2015). Gallic acid contained in fruits, plants, and derivate foods can be used for various biological applications due to its antiviral, antibacterial, and anticancer activity.

It was investigated in recent years for the coating of magnetic nanoparticles (MNP) aimed for biomedical applications in order to improve their biocompatibility (Shah et al., 2017).

We studied the gallic acid molecule and its interaction properties with water and other solvents aiming to use it further in the stabilization of magnetic nanoparticles in aqueous suspension – for biomedical applications.

II. QUANTUM CHEMICAL MODELING

The quantum chemical modeling of the gallic acid molecules in isolated as well as in hydrated state, was carried out in Spartan 18 software (Density Functional Theory method - B3-LYP/6-31G*(Bahdani et al., 2018).

III. EXPERIMENTAL

Electronic absorption spectra of pure gallic acid in various solvents (all reagents from SIGMA) and solvent mixtures were recorded with Shimadzu PharmaSpec UV 1700 device, in 1 cm quartz cells. The electro-optical macroscopic parameters of pure solvents in Table 1 are given: ε–the dielectric constant and n-the refractive index). For binary solvents $\varepsilon_{1,2}$ and $n_{1,2}$ were calculated according to formula $\varepsilon_{1,2} = f1*\varepsilon_1 + f2*\varepsilon_2$ where f1 and f2 are the volume fractions of the two pure solvents while ε_1, ε_2, n_1 and n_2 are their electro-optical macroscopic parameters.

No.	**TABLE 1-** Solvent prameters	ε	n
1	Toluene	2.34	1.496
2	Methylcyclohexanone	18	1.423
3	Chloroform	4.89	1.445
4	Isobutyl alcohol	17.93	1.395
5	Isopropyl alcohol	18.92	1.377
6	Ethanol	24.55	1.361
7	Methanol	32.66	1.328
8	Dimethylsulfoxide	48	1.479
9	Water	78.36	1.333

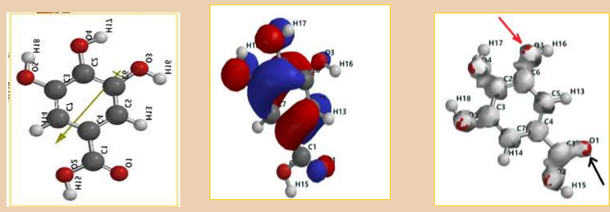
Solvatochromic study focused on the solvent influence on the gallic acid solute molecule was done based on the Lippert-Mataga model (Lippert, 1955) and Bakhshiev's one (Bakhshiev, 1962), that are considering the solvent macroscopic parameter effect on the electronic absorption band shift; they offer the possibility of estimating the solute molecule microscopic parameters in the excited state (such as the dipole moment) depending on the molecule parameters in the ground state – that can be obtained by quantum – chemical modeling (with DFT method in our case).

The gallic acid was used for stabilizing magnetite nanoparticles in aqueous suspension: 0.6 mM GA/g of MNP through magnetic stirring at 80 °C for 180 minutes (Szekeres et al., 2015). Co-precipitation method was used to synthesized magnetite nanoparticles according to Massart's method (1981).

The TEM technique (Transmission Electron Microscopy) was used (Hitachi High-Tech HT7700 device at 120 kV and 1 nm accuracy) to analyze the MNP stabilized by capping with gallic acid. The MNP size was estimated using the ImageJ software.

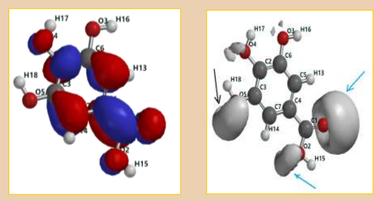
IV. RESULTS AND DISCUSSION

The results of quantum chemical modeling



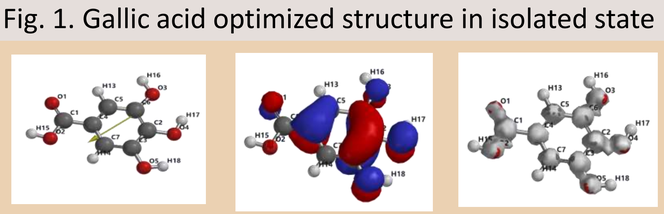
Dipole moment, HOMO orbital, ionizing potential map

Parameter	Isolated GA
E_{HOMO} (eV)	-5.99
E_{LUMO} (eV)	-1.06
Log P	-2.46
Dipole moment (D)	2.41
Polarizability	52.21



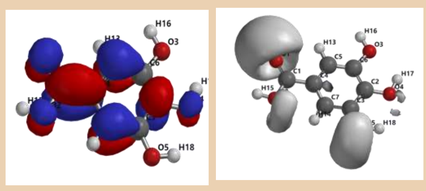
LUMO orbital, electrostatic potential map

Fig. 1. Gallic acid optimized structure in isolated state



Dipole moment, HOMO orbital, ionizing potential map

Parameter	Hydrated GA
E_{HOMO} (eV)	-5.97
E_{LUMO} (eV)	-1.15
Log P	-2.46
Dipole moment (D)	3.33
Polarizability	52.25



LUMO orbital, electrostatic potential map

Fig.2 Gallic acid structure in hydrated state

Also. molecule volume and surface were extracted from the computational modeling as necessary in the application of solvatochromic theory applications where molecule radius is needed (we have obtained 2.6 Å).

We noticed that the dipole moment in the hydrated state is enhanced with about 30% compared to the value corresponding to the isolated state of GA molecule.

The energies of the frontier orbitals are few changed by hydration , as well as the polarizability denoting preserving of the reactivity and stability.

In literature the GA modeling with PM3 (Parametrized Method 3) method resulted in the energies of the border electronic orbitals, E_{HOMO} = -9.31 eV și E_{LUMO} = -0.61 eV, as in the studies of Z. Lu et al., (2006) and S. Martinez et al, (2003) which attests good stability and reactivity with the chemical species from proximity (in solutions or suspensions).

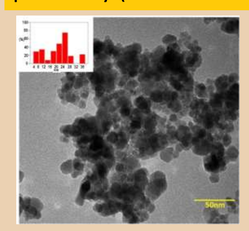


Fig. 3. TEM image of GA coated MNP in aqueous suspension

Fine granularity (around 15 nm) was found for the synthesized nanostructures confirming good interactions of GA molecule with iron ions at the MNP surface as well as the good solubility in water.

The results of solvatochromic study

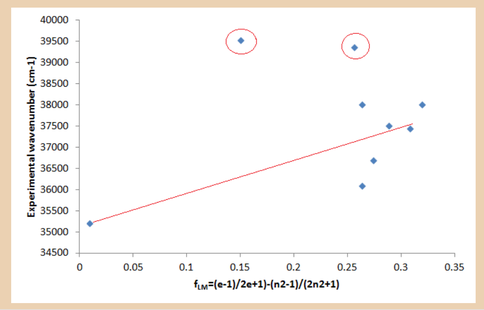


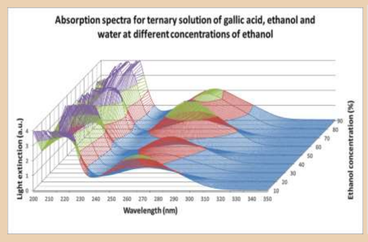
Fig. 4. Experimental wavenumber dependence on the pure solvents macroscopic parameters

Spectral shift toward higher wavenumbers was noticed for the increase of solvent dielectric constant. Lippert Mataga solvatochromic theory was applied to discuss the results.

$$\bar{\nu} = \frac{2(f_L(\varepsilon) - f_L(n))}{4\pi\varepsilon_0 hca^3}(\mu_g - \mu_e)^2 + \text{const.}$$

$$\Delta\bar{\nu} = \bar{\nu}_s - \bar{\nu}_0$$

where υ is the wavenumber of studied molecule in solution and υ_0 is of the isolated molecule (in vapor state), μ_g and μ_e are the dipole moments in the ground and excited state; *h* is Planck's constant, *c* is light velocity in the free space, *a* is the molecule radius. Best linear fitting was obtained by excepting chloroform and methylcyclohexanone that possibly developed specific solvent-solute interactions apart from universal volume interactions, developed by all solvents (in red circles). For solution concentration of about 10^{-4}M. The spectral shift, $\Delta\upsilon$ seems to depend linearly on the combined function fLM (of the dielectric constant and the refractive index). Dipole moment in the excited state resulted as equal of about 5.5 D.



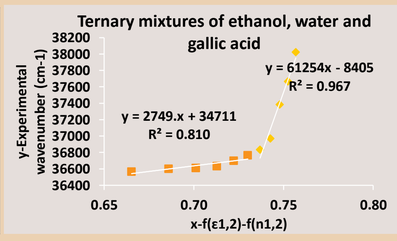
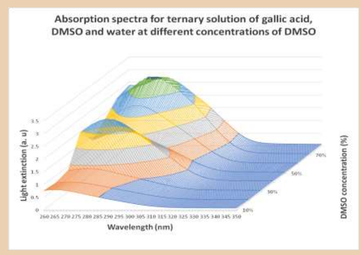


Fig. 5 Spectral behavior of GA solutions – with ethanol and water



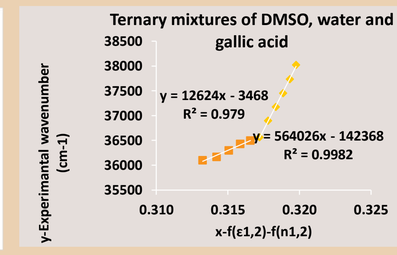


Fig. 6 Spectral behavior of GA solutions – with DMSO and water

In binary solvents similar behavior was evidenced with polar solvent surrounding GA molecule for low volume fractions of water while for large water volume fractions the GA molecule is surrounded mainly by water.

V. CONCLUSIONS. Gallic acid molecule revealed good interaction ability with surrounding molecules and MNP structures – as evidenced by TEM image of the final product. The quantum chemical simulation and the solvatochromic study in binary and ternary solutions allowed the revealing of universal interactions solute – solvent . The dipole moment in the excited state of GA molecule was calculated based on the quantum chemical modeling results and the results regarding the solvent effect on the wavenumber in the maximum of GA electronic absorption band in various pure solvents, Next research step is going to search for the evidencing of specific interactions developed by gallic acid in certain peculiar solvents.

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