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## Physico-chemical and biological properties of C<sub>60</sub>-L-hydroxyproline water solutions†

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This paper presents experimental data on a physico-chemical and biological study of C<sub>60</sub>-L-hydroxyproline derivative water solutions. The data on the temperature dependence of solubility in water, concentration dependences of density, specific conductivity, molar conductivity, and dissociation constants as well as experimental data on dynamic light scattering and biological effects on *in vitro* proliferation of cultured human epithelial kidney cells and *in situ* – on state of plants are presented and discussed.

### 1. Introduction

The relevance of studying derivatives of fullerenes with amino acids is mainly associated with their potential applications in biology and medicine.<sup>1–3</sup> We will briefly discuss the main results obtained in this area. Kotelnikova *et al.* studied the influence of water-soluble derivatives of C<sub>60</sub> with DL-alanine and DL-alanyl-DL-alanine on the structure and permeability of the lipid bilayer of liposomes based on phosphatidylcholine.<sup>4</sup> Hu *et al.* synthesized and characterized amphiphilic derivatives of C<sub>60</sub> with alanine, cysteine and arginine. It was revealed that these compounds can penetrate into the cell membrane and reduce the accumulation of reactive oxygen species (ROS) and cell injury caused by hydrogen peroxide in the pheochromocytoma cells (PC12).<sup>5</sup> Kumar *et al.* synthesized a conjugate of C<sub>60</sub> with lysine and studied the biological properties of the obtained compound.<sup>6</sup> It was shown that a C<sub>60</sub> – lysine derivative demonstrates a high effectiveness against cleavage of DNA upon irradiation with visible light in the presence of a reduced form of nicotinamide adenine dinucleotide (NADH). Jiang *et al.* synthesized a derivative of C<sub>60</sub> with glycine.<sup>7</sup> It was shown that the C<sub>60</sub> – glycine derivative leads to the death of cancer cells, and the effectiveness of the synthesized compound increases in a dose-dependent manner.<sup>7</sup> Authors of ref. 8 and 9 have explored the neuroprotective properties of hybrid structures based on C<sub>60</sub> and derivatives of proline. Kotelnikova *et al.* studied the antioxidant properties of water-soluble derivatives of C<sub>60</sub> with sodium salts of aminobutyric and aminocaproic acid.<sup>10</sup> The

authors revealed that amino acid derivatives are potential suppressors of cytomegaloviral infection.

Jennepalli *et al.* carried out the synthesis of mono and bis[60] fullerene-based dicationic peptoids.<sup>11</sup> The resulting hydrophobic, scaffolded di- and tetra-cationic derivatives were tested against *Staphylococcus aureus* NCTC 6571 and *Escherichia coli* NCTC 10418. Zhang *et al.* synthesized *N*-substituted, 3,4-fulleropyrrolidine according to the 1,3-dipolar cycloaddition of azomethine ylide and concluded that synthesized compounds would have unique properties and potential uses in medicine and biology.<sup>12</sup>

Additional groups of scientific articles are devoted to the theoretical study of fullerene derivatives with amino acids: (i) the ability of C<sub>60</sub> fullerene to interact with amino acids (the calculation was performed using DFT-B3LYP/3-21G);<sup>13</sup> (ii) calculation of the molecular structure of hybrid derivatives based on C<sub>60</sub> and amino acids using quantum-chemical methods;<sup>14</sup> and (iii) calculation of dissociation constants (pK<sub>a</sub>) of fullerene derivatives with amino acids.<sup>15</sup> A series of experimental papers devoted to the (i) investigation of pH, ionic strength and nature of the substituent influence on the C<sub>60</sub> – amino acids, peptides derivatives degree of association,<sup>16–21</sup> (ii) measuring of heat capacities of the amino acids and peptides derivatives aqueous solutions,<sup>22</sup> (iii) studying of temperature dependence of solubility in water, concentration dependences of density, specific conductivity, molar conductivity, dissociation constant, activity coefficients as well as size distribution in water solutions should also be mentioned.<sup>23–25</sup>

The present paper is devoted to a physico-chemical and biological investigation of water solutions of the C<sub>60</sub>-L-hydroxyproline derivative (C<sub>60</sub>-Hyp) (Fig. 1) — C<sub>60</sub>(C<sub>5</sub>H<sub>9</sub>NO<sub>3</sub>)<sub>2</sub> (isothermal and temperature dependences of the densities, concentration dependence of the refractive index, specific and molar conductivities, size distribution in water as well as the solubility of the C<sub>60</sub>-Hyp–water binary system and *in vitro*

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