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Functionalized C_{60} Fullerenes as Inorganic Redox Nanostructures: A Quantum Chemical Approach

A comprehensive quantum-chemical study of functionally modified C_{60} fullerenes ($C_{60}X_n$, n = 2, 4, 6) was performed using the hybrid PBE0 functional with dispersion correction (D4) and the SMD solvation model. Eighteen types of substituents with different electronic characteristics (X = $–CH_3$, $–C_2H_5$, $–C_3H_7$, –F, –Cl, –Br, –OH, $–OCH_3$, $–OC_2H_5$, –SH, $–SCH_3$, $–SC_2H_5$, $–NH_2$, $–NO_2$, –COOH, –COCl, $–CONH_2$, –CN) were attached to the fullerene structure to explore how their nature and number influence hydrophilicity, electronic structure, and antioxidant reactivity. The lipophilicity (log$P$), electronic chemical potential (μ), and reaction energy (ΔE) of superoxide ion deactivation were systematically analyzed. A correlation between μ and ΔE was revealed, showing that a decrease in μ enhances electron-accepting ability and antioxidant activity, although the relationship is modulated by the degree of substitution. The optimal balance between π-delocalization and electronic induction was found for tetra-substituted derivatives ($n = 4$). Electron-withdrawing groups ($–NO_2$, –CN, –COCl, –F, –Cl, –Br) significantly increased antioxidant efficiency, while alkyl and thioalkyl groups exhibited the opposite effect. The established relationships provide a quantitative framework for understanding redox behavior in carbon-based nanostructures and open prospects for the rational design of fullerene-derived antioxidants as inorganic molecular systems with tunable electronic properties.

Keywords: density functional theory, computer simulation, fullerenes, electronic chemical potential, antioxidant activity, structure-property relationship, inorganic nanomaterials, C_{60}

1 Introduction

Fullerenes are a special class of molecular carbon structures built from five- and six-membered cycles. The unique structural diversity and the resulting physico-chemical properties have made fullerenes and their functional derivatives the object of intensive research [1–15]. The study of fullerenes and their derivatives is of key importance for many modern technologies.

Due to their high antioxidant activity, they are used in biomedicine, where their potential as radioprotectors and anti-aging agents is being studied. Thus, due to the unsaturation of bonds between carbon atoms in fullerene molecules, their ability to exhibit antioxidant properties in relation to reactive oxygen species (ROS), for example, superoxide anion radicals O_2^-, is explained. However, fullerenes are lipophilic [2–6], nonpolar molecules, which complicates their transportation to the sites of ROS formation and accumulation.

To increase the solubility in water and reduce the logarithm of the distribution coefficient in the octanol-1 — water system (log$P$), which is 6.67 for fullerene C_{60} [2, 3], one can use ultrasonic dispersion of C_{60} dissolved in vegetable oil and polyvinyl alcohol [4].

Another, more effective method for increasing hydrophilicity involves chemical modification of the fullerene skeleton. To enhance hydrophilicity and solubility in an aqueous environment, fullerene molecules are modified with various polar and/or ionic groups (–OH, –COOH, –Cl, $–NH_2$, $–CH_2OCH_2–$, etc.) [2–8]. For example, in [5], synthesized C_{60}-aminocarboxylic acids were used to prevent apoptosis of rat PC12 cells induced by hydrogen peroxide. Greater viability was observed in cells treated with fullerene derivatives containing arginine and β-alanine residues. The latter derivative is recommended as a cell protector due to its greater solubility in both water and non-polar media. Similar results for C_{60} derivatives were confirmed amperometrically in [6]. In [7], C_{60} modified with proline and other functional groups (nitroalkyl, hydroxyalkyl, maleimide, carnosine) was studied. Proline provided hydrophilicity to the nanostructure, while other groups (including the fullerene backbone) provided biological activity: antiviral, antioxidant, and antitumor. It was noted that a derivative with carnosine, which is also an antioxidant, has an increased ability to interact with radicals. In the work [8], the influence of the lipophilicity of fullerene C_{60}, modified with amino acids with different contents of lyophilic and hydrophilic fragments, on the ability to inhibit lipid oxidation in an aqueous environment is studied using the chemiluminescence method. Rat brain homogenate was used as a lipid, *tert*-butyl hydroperoxide was the source of radicals, and the reaction was carried out in an aqueous medium in the presence of luminol. As a result, it was established that less hydrophilic derivatives, which can more easily penetrate the phospholipid and act as an ROS scavenger, have high inhibition efficiency. An increase in functional groups in fullerene molecules not only increases their solubility in water, but also reduces their antioxidant activity, which was demonstrated in the study of hydroxyfullerenes $C_{60}(OH)_n$, where $2 \leq n \leq 26$ [9], and others [2, 5, 7].

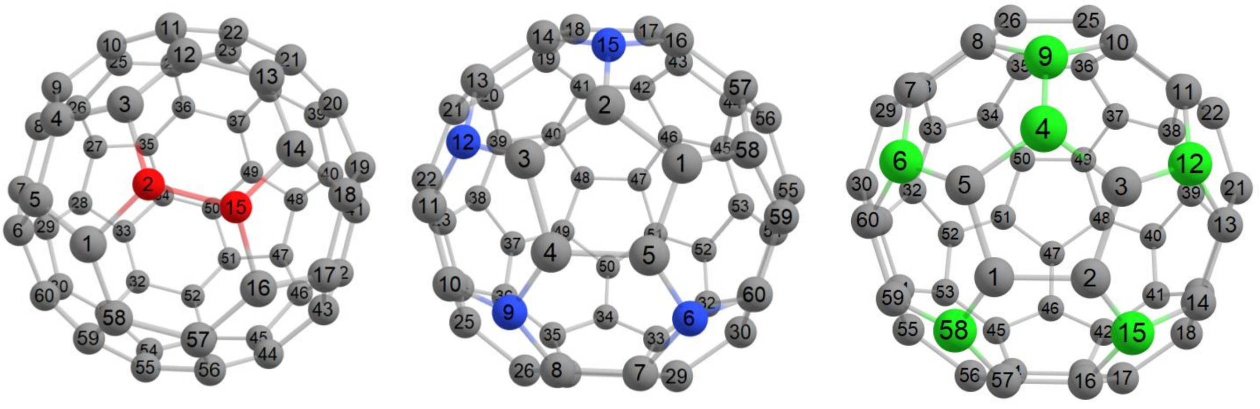
The antioxidant and lipophilic properties of fullerene molecules and their derivatives are also studied using quantum chemistry and computer modeling, complementing experiments. Quantum-chemical calculation methods have proven themselves to be effective theoretical methods for predicting properties. These calculations, based on density functional theory (DFT), have become a powerful tool for studying the reactivity of fullerenes. They have been used to study radical reactions [10] and the ozone addition process [11]. In [12–14], various quantum-chemical approaches to modeling the structure of fullerenes and estimating the energy of isomeric structures were considered and evaluated. It was shown that quantum-chemical modeling of such atomic-molecular systems has a high accuracy. In work [15], the DFT method was used to determine the energies of interaction of C_{60} with molecules of aminocarboxylic acids in the gas phase, and a hypothesis was put forward about the correlation of the thermodynamic functions of the formation of adducts of fullerenes with amino acids and the lipophilicity coefficient.

The accumulated experimental and theoretical information on the antioxidant properties of fullerenes and the effect of substituents on the lipophilicity of nanostructures based on them are one of the key points for the targeted design of nanomaterials, since the question remains to what extent it is advisable to reduce the hydrophobicity of fullerenes. There is also a question about the number of substituents on the fullerene backbone (more substituents means better solubility, but less activity as an ROS scavenger). Therefore, further study of the relationship between lipophilicity, antioxidant activity and electronic structure of fullerene derivatives is required. The purpose of this study is to perform quantum chemical modeling and compare a number of C_{60} fullerene derivatives modified with two, four, and six identical substituents of different electronic nature (X), both electron-donating and electron-acceptor (X = $–CH_3$, $–C_2H_5$, $–C_3H_7$, –F, –Cl, –Br, –OH, $–OCH_3$, $–OC_2H_5$, –SH, $–SCH_3$, $–SC_2H_5$, $–NH_2$, $–NO_2$, –COOH, –COCl, $–CONH_2$, –CN), to establish the relationships between the structure of molecules, their electronic structure, lipophilicity and antioxidant activity (the ability to accept an electron from a superoxide ion O_2^-, converting it into a safer triplet oxygen O_2).

2 Computational Details

2.1 Parameters of Quantum Chemical Computer Simulation

Among the variety of $C_{60}X_n$ isomers, one stable isomer of each series was selected [16]. The model of the C_{60} fullerene frame with the atom numbering used is shown in Figure 1. Functional groups were attached to the following C atoms: $C_{60}X_2$ (2, 15); $C_{60}X_4$ (6, 9, 12, 15); $C_{60}X_6$ (4, 6, 9, 12, 15, 58).



a *b* *c*

a — attachment of two X groups to red carbon atoms; *b* — attachment of four X groups to blue carbon atoms;
c — attachment of six X groups to green carbon atoms

Figure 1. Designations of the positions of attachment of functional groups to the fullerene C_{60}

Computer modeling was performed in the ORCA 6.1 software package [17] using the hybrid density functional PBE0 as a calculation method [18]. It optimally combines an accurate account of the electronic structure of the π-system of the fullerene backbone and a reliable description of the energy of interaction with functional groups, including non-covalent interactions. To accurately describe the weak non-covalent interactions (for example, van der Waals forces) that can be significant in substituted fullerenes, especially with bulky alkyl chains, the D4 empirical dispersion correction scheme by Grimme and coworkers [19] was employed in conjunction with PBE0. This addition is critical for obtaining realistic structures and energies.

A dual-basis set strategy was adopted to ensure both efficiency and accuracy. The def2-SVP basis set [20] was used for geometry optimizations and frequency calculations. This basis offers a good compromise, providing reliable structural parameters for large molecules at a reasonable computational cost. For more accurate single-point energy calculations (essential for deriving electronic potentials and energies), the larger def2-TZVPD basis set was employed [20, 21]. This triple-zeta quality basis set, augmented with diffuse functions, is crucial for correctly describing electron affinities, ionization potentials, and anionic species (such as $C_{60}X_n^-$, O_2^-) involved in the antioxidant activity assessment [22].

2.2 The Octanol-Water Partition Coefficient (logP)

The octanol-water partition coefficient logP reflects the ability of a substance to be distributed between nonpolar (octanol) and polar (water) media (Equation 1):

$$P(\mathrm{C}_{60}\mathrm{X}_n)=\frac{[\mathrm{C}_{60}\mathrm{X}_n]_o}{[\mathrm{C}_{60}\mathrm{X}_n]_w} \qquad (1)$$

The higher the log*P*, the more lipophilic the structure is. The lipophilicity coefficient was estimated using the chemical reaction isotherm equation (Equation 2) [23]:

$$\Delta G_{w\to o}(\mathrm{C}_{60}\mathrm{X}_n)=2.303RT\log P(\mathrm{C}_{60}\mathrm{X}_n)\,, \qquad (2)$$

where $\Delta G_{w\to o}$ is the change in the Gibbs function of the transition process of a fullerene molecule from an aqueous medium to an octanol medium, J/mol; *R* is the universal gas constant, J/(mol·K); *T* is the temperature, K.

Here, the calculated lipophilicity coefficient of the modified fullerene was subtracted from the calculated lipophilicity coefficient of pure fullerene in order to be able to compare the lipophilicity and hydrophilicity of structures after modification and eliminate possible errors of the method and the basic set when comparing (Equation 3):

$$\Delta\log P(\mathrm{C}_{60}\mathrm{X}_n)=\log P(\mathrm{C}_{60}\mathrm{X}_n)-\log P(\mathrm{C}_{60})=\frac{\Delta G^0_{w\to o,298}(\mathrm{C}_{60})-\Delta G^0_{w\to o,298}(\mathrm{C}_{60}\mathrm{X}_n)}{2.303RT}\,. \qquad (3)$$

The energies of molecules in an aqueous medium and an octanol medium were calculated using the continuous solvent model SMD [23]. The geometry of the molecules was optimized in each solvent (water and octanol) using the def2-SVP basis. To evaluate the Gibbs functions of the transition of molecules from water to octanol ($\Delta G_{w\to o,298}{}^{0}$), the single-point energies ($FSP_{\text{(water)}}$, $FSP_{\text{(octanol)}}$) of these structures in water and in octanol were calculated, and thermal corrections were calculated taking into account the oscillation frequencies at $T = 298.15$ K and $p = 1$ atm ($\Delta E_{\text{(water)}}$, $\Delta E_{\text{(octanol)}}$,) for pure fullerene and its derivatives (Equation 4). The FSPs were calculated using the def2-TZVPD basis set, and the thermal corrections were calculated using the def2-SVP basis set:

$$\Delta G^{0}_{w\to o,298}(\mathrm{Y}) = FSP_{\text{(octanol)}}(\mathrm{Y}) - FSP_{\text{(water)}}(\mathrm{Y}) + \Delta E_{\text{(octanol)}}(\mathrm{Y}) - \Delta E_{\text{(water)}}(\mathrm{Y}), \tag{4}$$

where Y is the C_{60} and $C_{60}X_n$.

It is important to note that the absolute calculated log*P* value for unsubstituted C_{60} (9.06) overestimates the experimental value (6.67) [24]. According to the isotherm Equation 2, the error is 13.6 kJ/mol (0.14 eV), which is an acceptable error for calculating energies in continuous solvent models for large and voluminous, as well as highly hydrophobic molecular structures [25], such as pure unmodified fullerene. Therefore, to ensure the reliability of our structure-property analysis, we focus exclusively on the relative lipophilicity parameter, Δlog*P*. This relative scale effectively cancels out systematic errors in the solvation energy calculations for the common fullerene core, allowing for a robust comparison of the substituent effects.

Antioxidant Activity of Functionally Modified Fullerenes in Relation to Superoxide Ion

The antioxidant activity of modified $C_{60}X_n$ fullerenes (n = 2, 4, 6) was evaluated by the reaction of the fullerene structure with the superoxide ion, assuming the mechanism of electron transfer from the superoxide ion with its oxidation to molecular oxygen:

$$C_{60}X_n + O_2^- \rightarrow C_{60}X_n^- + O_2$$

The reaction energy ΔE was calculated according to Hess's law based on single point energies (Final Single Point Energy — *FSP*). Negative values of ΔE correspond to spontaneous reaction and high antioxidant activity

$$\Delta E = FSP(C_{60}X_n^-, opt) + FSP(O_2, opt) - FSP(C_{60}X_n, opt) - FSP(O_2^-, opt) \tag{5}$$

For the reaction energy ΔE, full geometry optimizations were performed for all species: neutral $C_{60}X_n$, O_2, radical anions $C_{60}X_n^-$, O_2^-. The optimizations were carried out at the PBE0-D4/def2-SVP/SMD(Water) level. FSP energies were then calculated with the def2-TZVPD basis set to obtain accurate energies.

For the structures in equation 5, the following values of charge (*C*) and spin multiplicity (*M*) were used: $C_{60}X_n$ ($C = 0$, $M = 1$); $C_{60}X_n^-$ ($C = -1$, $M = 2$); O_2^- ($C = -1$, $M = 2$); O_2 ($C = 0$, $M = 3$). All energies of the optimized neutral and anionic structures are listed in the Supplementary Materials (Table S1).

2.4 Electronic Chemical Potentials of Structures C60Xn

The electron chemical potential μ was chosen as a measure of the acceptor capacity of fullerene structures, which was calculated using the apparatus of the conceptual density functional theory (CDFT) [26]. The electronic chemical potential is a change in the energy of an atomic-molecular system (*E*) when an electron (*N*) is attached while the geometry of the structure remains constant (conservation of the nuclear potential V_n = const):

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{Vn=const} \approx -\frac{I + A}{2} \tag{6}$$

In equation (6), *I* is the vertical ionization energy, and *A* is the vertical electron affinity of fullerene structures. They were calculated using equations (7) and (8), respectively:

$$I = FSP(C_{60}X_n^+) - FSP(C_{60}X_n), \tag{7}$$

$$A = FSP(C_{60}X_n) - FSP(C_{60}X_n^-). \tag{8}$$

The descriptor (μ) shows the ability of a structure to participate in donor-acceptor interactions and the ability to shift the electron density from another structure. When a system of interacting structures is formed, the electron density will predominantly flow to the structure with a more negative value of μ.

Cartesian coordinates and total energies for all structures are available in the Supplementary Materials (Table S2).

3 Results and Discussion

3.1 The Octanol-Water Partition Coefficient (logP)

log*P* is one of the key parameters in QSAR (Quantitative structure — activity relationship) and medicinal chemistry, as it reliably predicts the ability of a molecule to passively transport across biological membranes, its solubility, and overall bio-distribution *in vivo*. In this work, the relative hydrophobicity parameter (Δlog*P*), showing a change in hydrophobicity compared to unmodified C_{60} fullerene. This systematic approach allows for a detailed analysis of the effect of the nature and number of functional groups on the lipophilic properties of the fullerene framework. Figure 2 shows a heat map visualizing the effect of functional groups and the degree of substitution on the hydrophobicity of $C_{60}X_n$ fullerene derivatives relative to unmodified C_{60}.

Data analysis reveals several clear patterns:

1) The heat map shows a pronounced division of functional groups into two opposite clusters. Powerful hydrophobizers are located in the upper part: propyl- ($–C_3H_7$) and thioethyl- ($–SC_2H_5$) groups demonstrate the most significant increase in lipophilicity (Δlog*P* to +5.86 and +5.92 at $n = 6$, respectively). Hydrophilic groups are concentrated in the lower part, and the carboxyamide group ($–CONH_2$) exhibits the strongest hydrophilic effect (Δlog*P* up to –9.12 at $n = 6$);

2) A significant dependence is observed for most groups: an increase in the degree of substitution from $n = 2$ to $n = 6$ leads to an increase in the initial effect of the group. For most of the functional groups studied (for the simulated positions of groups on the fullerene framework), a distinct linear dependence of Δlog*P* on the degree of substitution n is observed. So, for the groups $–C_3H_7$, –F, –Cl, –SH, $–SCH_3$, $–SC_2H_5$, $–NH_2$, –COOH and $–CONH_2$, the correlation coefficient $R^2 > 0.99$. For the groups $–CH_3$, $–C_2H_5$, –Br, –OH, –COCl, –CN and $–NO_2$, the correlation coefficient $R^2 > 0.9$. For the groups $–OCH_3$ ($R^2 = 0.39$) and $–OC_2H_5$ ($R^2 = 0.22$), due to the peculiarities of their location on the fullerene framework, a strong nonlinear dependence is observed. The nonlinear behavior of certain groups is explained by a complex balance of steric, electronic, and solvation effects, which are not a simple sum of the contributions of individual substituents;

3) The ranking of groups by their effect on lipophilicity shows that the amide group ($–CONH_2$) is the most powerful hydrophilizer. Among hydrophobizers, groups with long hydrocarbon chains and thioalkyl substituents are most effective.

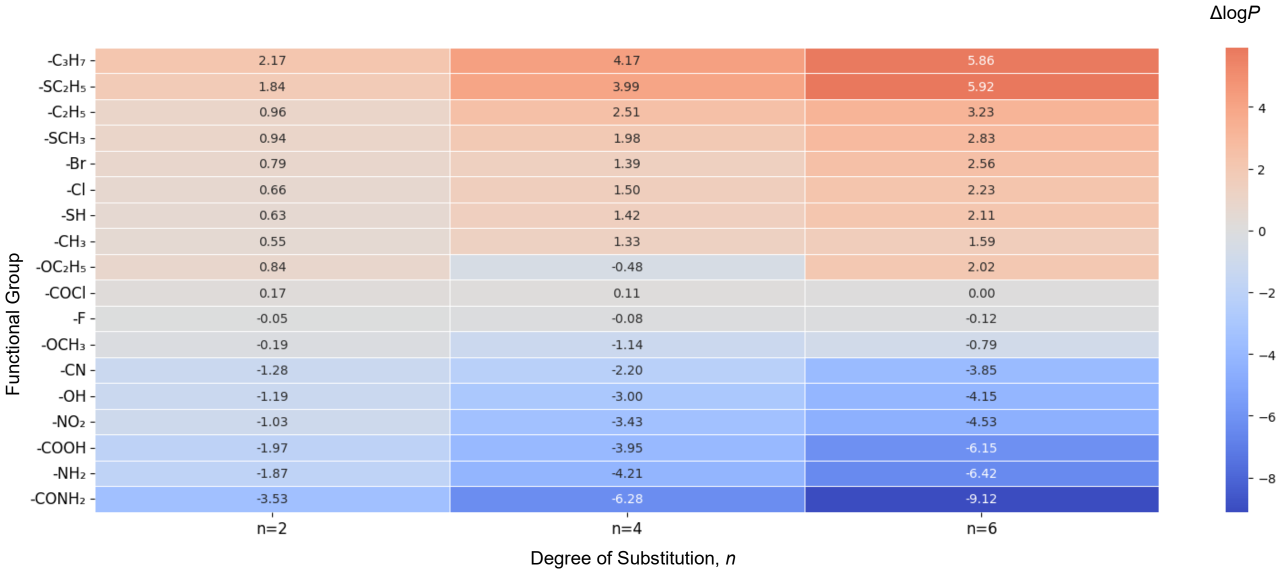


Figure 2. Heat map of the relative change in hydrophobicity (Δlog*P*) of functionally substituted $C_{60}X_n$ fullerenes calculated by quantum chemical methods relative to unmodified C_{60} fullerene (blue tones — more negative values of Δlog*P*, low hydrophobicity; red tones — more positive values of Δlog*P*, high hydrophobicity)

As can be seen from the analysis of the Δlog*P* dependence, the nature and number of functional substituents have a systematic effect on the hydrophobicity of the fullerene structure. Since hydrophobicity determines not only the solubility and transport of a molecule in biological media, but also the effectiveness of interaction with radical oxygen forms, it seems logical to compare these data with the electronic characteristics and antioxidant activity of the obtained structures. In particular, it can be expected that an increase in hydrophilicity (a decrease in log*P*) due to the introduction of electron acceptor groups will be accompanied by a decrease in the electron chemical potential and an increase in the ability of the molecule to accept an electron from the superoxide ion. Thus, the transition from the analysis of ΔlogP to the assessment of antioxidant activity allows us to move from the macroscopic characteristics of solubility to the quantum chemical description of reactivity.

3.2 Antioxidant Activity of Functionally Modified Fullerenes in Relation to Superoxide Ion

The antioxidant activity of modified $C_{60}X_n$ fullerenes ($n = 2, 4, 6$) was evaluated by the equation 5. Figure 3 shows a heat map of the ΔE values for all 54 derivatives studied. In the case of calculating the reaction energy (5) for unmodified fullerene C_{60}, we obtained a value of $\Delta E = -35.2$ kJ/mol. It is clearly seen that antioxidant activity depends non-linearly on both the nature of substituent X and the degree of functionalization *n*. For most compounds, a minimum of ΔE (the highest activity) is observed at $n = 4$, whereas at $n = 2$ and $n = 6$, the reaction becomes less advantageous. This effect is explained by the balance between the preservation of the delocalized π-system of the fullerene framework and the induction effect of substituents. It is important to note that in this study, the influence of the nature of the functional group on the properties of the fullerene structure was studied in the context of a single isomer in each series $n = 2, 4, 6$.

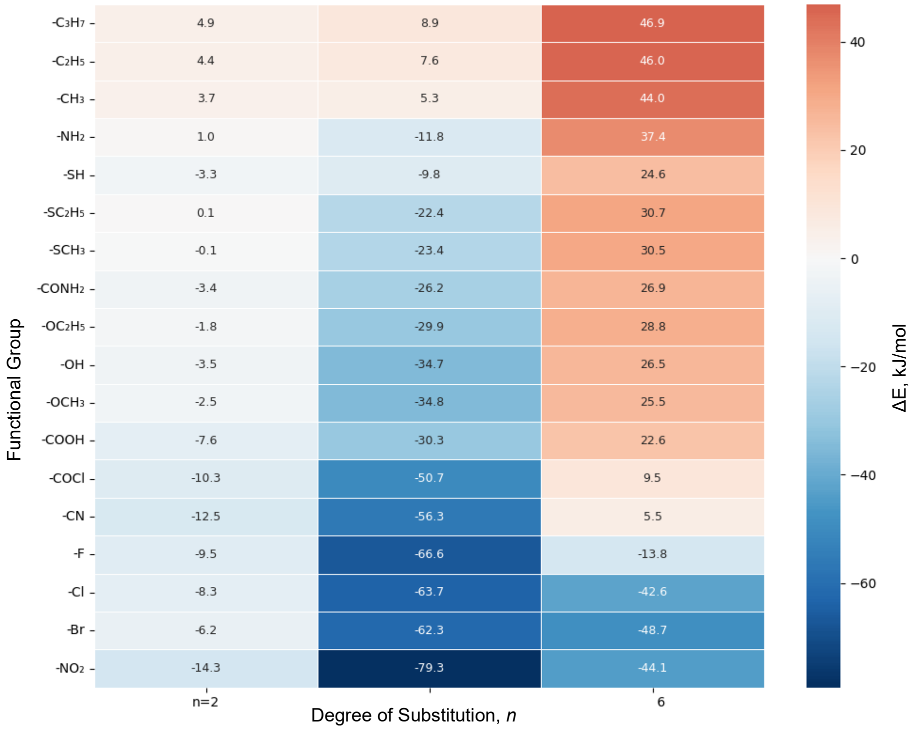


Figure 3. Heat map of reaction energy values ΔE (kJ/mol) for modified fullerenes $C_{60}X_n$ ($n = 2, 4, 6$) in reaction with the superoxide ion O_2^-. The color scale reflects the thermodynamic benefits of the process (blue tones — more negative values of ΔE, high antioxidant activity; red tones — more positive values of ΔE, low activity)

The maximum antioxidant activity is typical for compounds containing electron acceptor groups –F, –Cl, –Br, $-NO_2$, –CN and –COCl (ΔE from –40 to –80 kJ/mol at $n = 4$). These substituents lower the electron chemical potential of μ to –5.8÷–5.9 eV, which reflects their high ability to accept an electron. Electron-donating groups (alkyl, alkoxy, thioalkyl, and amino groups) exhibit the opposite effect: they increase the μ (up to –4.4 eV) and make the reaction less advantageous ($\Delta E > 0$).

3.3 Electronic Chemical Potentials of Structures $C_{60}X_n$

The electronic chemical potential (μ) is one of the key parameters of the conceptual theory of the density functional, reflecting the general tendency of a molecule to receive or give electrons. More negative values of μ correspond to more pronounced electron-withdrawing properties and, consequently, a greater tendency of the system to reduction. Table shows the calculated values of electronic chemical potentials μ for CDFT $C_{60}X_n$ structures according to equation 6.

The lowest values of μ are observed for structures containing electron acceptor groups –CN, $–NO_2$, –COCl, –F, –Cl, and –Br, which reflects the pronounced acceptor effect of these substituents on the π-electron system of the fullerene framework. The decrease in μ is especially noticeable during the transition from $n = 2$ to $n = 4$, which indicates an increase in the electron acceptor effect with an increase in the degree of functionalization. With a further increase in the number of substituents to $n = 6$, only a slight increase in μ is observed, which can be explained by the partial destabilization of the π-system due to oversaturation of the fullerene framework.

Table

Values of electronic chemical potentials μ (eV) of $C_{60}X_n$ structures

Group X									
n	CN	NO_2	COCl	F	Cl	Br	OH	COOH	$CONH_2$
2	–5.45	–5.41	–5.28	–5.24	–5.20	–5.17	–5.09	–5.07	–5.06
4	–5.95	–5.90	–5.41	–5.32	–5.27	–5.23	–5.12	–5.15	–5.15
6	–5.88	–5.83	–5.41	–5.39	–5.30	–5.30	–4.92	–4.89	–4.87
Group X									
n	SH	OCH_3	OC_2H_5	SCH_3	SC_2H_5	NH_2	CH_3	C_2H_5	C_3H_7
2	–5.07	–5.03	–5.00	–4.98	–4.95	–4.97	–4.92	–4.89	–4.87
4	–5.04	–5.09	–5.11	–5.03	–4.98	–4.80	–4.82	–4.84	–4.75
6	–4.94	–4.78	–4.70	–4.74	–4.65	–4.63	–4.51	–4.45	–4.42

For the moderately polar groups –OH, –COOH, and $–CONH_2$, the values of μ are close to the potential of unmodified C_{60} (–5.19 eV). These substituents have a weak acceptor effect without disturbing the electronic structure of the fullerene. On the opposite end of a number are electron-releasing substituents — alkyl ($–CH_3$, $–C_2H_5$, $–C_3H_7$), the alkoxy- and thioalkyl group ($–OCH_3$, $–OC_2H_5$, $–SCH_3$, $–SC_2H_5$) and amino group ($–NH_2$). For them, μ increases sequentially with increasing length of the alkyl chain or degree of substitution. This reflects an increased donor effect and an increase in the electron density on the fullerene framework. Thus, the distribution of μ values makes it possible to divide the studied functional groups into three main classes according to the nature of electronic influence:

1) strong acceptors ($–NO_2$, –CN, –COCl, –F, –Cl, –Br);
2) temperate polar groups (–OH, –COOH, $–CONH_2$);
3) donors (alkyl, alkoxy, thioalkyl, amino groups).

This classification reflects the general electronic structure of fullerene derivatives and forms the basis for subsequent analysis of their reactivity. Since μ is directly related to the thermodynamic characteristics of the reduction processes, a further comparison of the obtained values with the energies of the superoxide ion (ΔE) capture reaction makes it possible to establish patterns between the electronic structure and the antioxidant activity of fullerenes. For all the studied series of fullerene derivatives $C_{60}X_n$ ($n = 2, 4, 6$), a clear relationship was revealed between the energy of the superoxide ion deactivation reaction (ΔE) and the electronic chemical potential μ calculated using the conceptual density functional theory (Figures 4 and 5). The red dashed line in these figures at a value of $\mu = 5.19$ eV shows the numerical value for pure unmodified fullerene C_{60}.

According to the data in Figure 4, it can be seen that, in general, with a decrease in the chemical potential (with an increase in the ability of the fullerene structure to accept electrons), antioxidant activity increases. The dependence is far from linear, as indicated by the low correlation coefficient ($R^2 = 0.5543$). But the following trend is observed. Practically all the structures studied, which have an μ value that is more negative than that of pure fullerene (to the left of the red dashed line), have increased antioxidant activity with respect to the superoxide ion compared to pure fullerene. This can be explained by the fact that the deactivation of the superoxide ion according to the reaction scheme (5) occurs by the electron transfer mechanism, and the fullerene structure acts as an electron acceptor. More negative values of the chemical potential give the structure more acceptor properties.

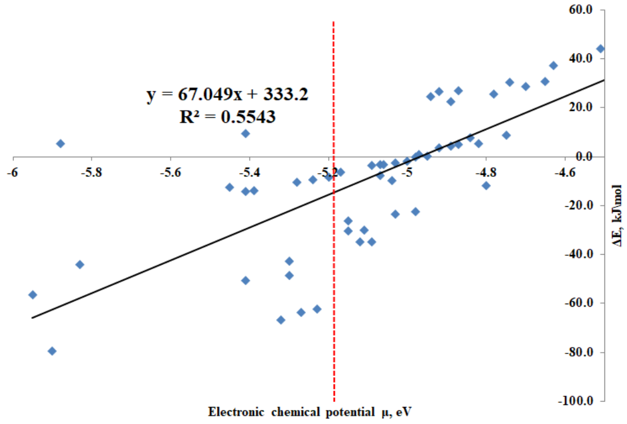


Figure 4. Dependence of the antioxidant activity of fullerene structures $C_{60}X_n$ with respect to the superoxide ion (ΔE) on the electronic chemical potential μ without differentiation by series of derivatives

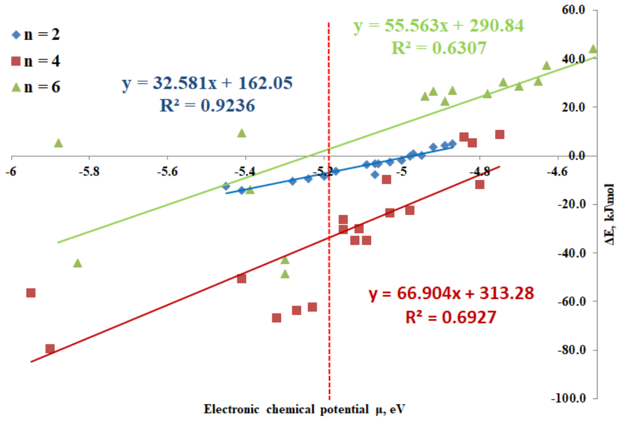


Figure 5. Dependence of the antioxidant activity of fullerene structures $C_{60}X_n$ with respect to the superoxide ion (ΔE) on the electronic chemical potential μ with differentiation by three series of derivatives: $n = 2$, $n = 4$, $n = 6$

A clearer picture is observed if we differentiate the values in Figure 4 by three series of derivatives ($n = 2$, $n = 4$ and $n = 6$). The most linear dependence is inherent in $C_{60}X_2$. Such a small number of groups, even being in close proximity to each other with neighboring carbon atoms of the fullerene framework, do not significantly distort the linearity and additivity of antioxidant properties ($R^2 = 0.9236$). The more groups are fixed on fullerene, the greater the deviations from linearity ($n = 4$, $R^2 = 0.6927$; $n = 6$, $R^2 = 0.6307$). But in general, the trend originally outlined in Figure 4 is also evident here separately in three series of derivatives: with a decrease in chemical potential, antioxidant activity increases.

4 Conclusions

A comprehensive quantum-chemical study of 54 functionalized $C_{60}X_n$ ($n = 2, 4, 6$) derivatives was performed using the hybrid PBE0 functional with dispersion correction. In this work, the properties of modified fullerenes, such as hydrophilicity, electronic chemical potential as a measure of the structure's ability to transfer electron density, and the oxidizing capacity of modified fullerenes towards the active form of oxygen, the superoxide ion, were modeled.

Electronic nature and number of substituents systematically determine the hydrophilicity, electronic properties, and antioxidant activity of the fullerene framework. Hydrophilicity increases with the introduction of electron-withdrawing substituents ($-NO_2$, $-CN$, $-COCl$, $-F$, $-Cl$, $-Br$), while alkyl and thioalkyl groups act as strong hydrophobizers. Optimal antioxidant activity is achieved for tetra-substituted derivatives ($n = 4$), where the π-system remains sufficiently delocalized, and the electron-accepting effect of substituents is maximal. The reaction energy (ΔE) for the deactivation of the superoxide ion O_2^- correlates inversely with the electronic chemical potential μ, indicating that the lowering of μ enhances electron affinity and antioxidant reactivity. Moderately polar groups ($-OH$, $-CONH_2$, $-COOH$) exhibit balanced solubility and redox behavior, making them promising candidates for biomedical fullerene derivatives with tunable antioxidant efficiency.

Overall, the results establish quantitative structure–property relationships connecting hydrophilicity, electronic potential, and thermodynamic reactivity, offering a rational framework for the molecular design of fullerene-based antioxidants.

Supporting Information

The Supporting Information is available free at https://ejc.buketov.edu.kz/ejc/article/view/567/392

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Conflicts of Interest

The authors declare no conflict of interest.

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