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Structural relationships and theoretical study of the free energies of electron transfer, electrochemical properties, and electron transfer kinetic of cephalosporin antibiotics derivatives with fullerenes in nanostructure of [R]·C$_n$ (R = cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone) supramolecular complexes

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Abstract Various empty carbon fullerenes (C$_n$) with different carbon atoms have been obtained and investigated. Cephalosporin antibiotics and its derivatives have important medicinal properties. The β-lactam class of antibiotics has a broad spectrum of antimicrobial properties. Their antibacterial and pharmacokinetic properties have wide therapeutic applications. Topological indices have been successfully used to construct effective and useful mathematical methods to establish clear relationships between structural data and the physical properties of these materials. In this study, the number of carbon atoms in fullerenes was used as an index to establish a relationship between the structures of cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone (β-lactam antibiotics) and fullerenes (C$_n$, n = 60, 70, 76, 82 and 86), which create [cefadroxil]·C$_n$, [cefepime]·C$_n$, [cephalexin]·C$_n$, [cefotaxime]·C$_n$, [cefoperazone]·C$_n$ and [ceftriaxone]·C$_n$. The relationship between the number of fullerene carbon atoms and the free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) are assessed using the Rehm-Weller equation for **A-1** to **A-5**, **B1** to **B-5**, **C-1** to **C-5**, **D-1** to **D-5**, **E-1** to **E-5** and **F-1** to **F-5** of the supramolecular complexes [R]·C$_n$ (where R = cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone) complexes. The calculations are presented for the four reduction potentials ($^{Red.}E_1$–$^{Red.}E_4$) of fullerenes C$_n$. The results were used to calculate the four free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of the cephalosporin-fullerene supramolecular complexes **A-1** to **A-5**, **B1** to **B-5**, **C-1** to **C-5**, **D-1** to **D-5**, **E-1** to **E-5** and **F-1** to **F-5** for fullerenes C$_{60}$–C$_{120}$. The free energies of activation for electron transfer, $\Delta G_{et(n)}^{\#}$ (n = 1–4) were also calculated for these complexes in accordance with the *Marcus* theory. In this study, was presented the calculated wavelengths ($\lambda_{(n)}$; n = 1–4; in nm) of the photoelectron transfer process as well in the nanostructure complexes.

Keywords Fullerenes · Cephalosporin antibiotics · Rehm-Weller equation · Free energy of electron transfer · Electron transfer properties · Activated free energies of electron transfer · Marcus theory · Planck's equation · Molecular modeling

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Introduction

Developments in nanoscience and nanotechnology have opened the field to tremendous theoretical and experimental advances in various fields, including biomedical sciences [1–10]. The pharmacokinetic properties of

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cephalosporin antibiotics are nearly identical [11–13]. Cephalosporins consist of a fused β-lactam-Δ^3-dihydrothiazine two-ring system known as 7-aminocephalosporanic acid (7-ACA) and vary in their side chain substituents [11]. Cephalosporin derivatives vary in their resistance to β-lactamases. Despite relatively extensive knowledge of these drugs, their qualitative and quantitative analyses still give rise to many problems. These difficulties are due to the chemical instability of the common β-lactam nucleus and minor differences in the chemical structures of the analogs. These structures are classified into four generations based on their resistance to β-lactamase degradation. Cephalosporins have an added advantage in that the penicillin-allergic patients can be treated with these antibiotics [11–14]. Here, cefadroxil (1, first class), cefepime (2, fourth class), cephalexin (3, first class), cefotaxime (4, third class), cefoperazone (5, third class) and ceftriaxone (6, third class) were selected for the aims and viewpoints of this study.

Cefadroxil is a broad-spectrum bactericidal antibiotic of the cephalosporin type and is effective to treat Gram-positive and Gram-negative bacterial infections [15]. Cefadroxil is a first-generation cephalosporin antibacterial drug that is a para-hydroxy derivative of cephalexin, and it has been used similarly in the treatment of mild to moderate susceptible infections, such as the bacterium *Streptococcus pyogenes*, which causes strep throat. Cefadroxil is used as an antibiotic prophylaxis before dental procedures and can be used for treating infected wounds on animals [15].

Cefepime is a fourth-generation cephalosporin antibiotic developed in 1994. Cefepime has an extended spectrum of activity against Gram-positive and Gram-negative bacteria [15–18]. The combination of the syn-configuration of the methoxyimino moiety and the aminothiazolyl moiety confers extra stability to β-lactamase enzymes produced by many bacteria. These factors increase the activity of cefepime against otherwise resistant organisms, including *Pseudomonas aeruginosa* and *Staphylococcus aureus* [15–18].

Cephalexin is a first-generation cephalosporin antibiotic, introduced in 1967 by Eli Lilly and Company [19], and it has similar antimicrobial spectrum to the intravenous agents such as cefalotin and cefazolin. Cephalexin treats urinary tract infections, respiratory tract infections and skin and soft tissue infections. Cephalexin has been used to treat acne, and it is a useful alternative to penicillin derivatives in patients with penicillin hypersensitivity. Cephalexin and other first-generation cephalosporins are known to have a modest cross-allergy in patients with penicillin hypersensitivity [11–15, 19].

Cefotaxime is a third-generation cephalosporin antibiotic. Like other third-generation cephalosporins, Cefotaxime has a broad spectrum of activity against Gram-positive and Gram-negative bacteria [20]. The stability of the β-lactamases increases the activity of cefotaxime against otherwise resistant Gram-negative organisms [20]. Cefotaxime is used to treat infections of the respiratory tract, skin, bones, joints, urogenital system, meningitis and septicemia. Cefotaxime is active against penicillin-resistant strains of *Streptococcus pneumoniae* and has modest activity against the anaerobic bacteria *Bacteroides fragilis*. Cefotaxime, like other β-lactam antibiotics, blocks the division of bacteria (including cyanobacteria), the division of cyanelles (the photosynthetic organelles of the glaucophytes) and the division of chloroplasts in bryophytes [11–13, 20].

Cefoperazone is a third-generation cephalosporin antibiotic, marketed by Pfizer, and it is one of the few cephalosporin antibiotics effective in treating *Pseudomonas* bacterial infections which are otherwise resistant to these antibiotics [11–13, 21]. Cefoperazone exerts its bactericidal effect by inhibiting bacterial cell wall synthesis, and sulbactam acts as a β-lactamase inhibitor to increase the antibacterial activity of cefoperazone against β–lactamase-producing organisms [11–13, 21]. Cefoperazone contains an *N*-methylthiotetrazole (NMTT) side chain. As the antibiotic is broken down in the body, free NMTT is released, which can cause hypoprothrombinemia (likely due to the inhibition of the enzyme vitamin K epoxide reductase) and a reaction with ethanol similar to that produced by disulfiram (Antabuse) due to inhibition of aldehyde dehydrogenase [11–13, 21].

Ceftriaxone is a third-generation cephalosporin antibiotic. Like other third-generation cephalosporins, ceftriaxone has a broad spectrum of activity against Gram-positive and Gram-negative bacteria. In most cases, ceftriaxone is considered to be equivalent to cefotaxime in terms of safety and efficacy [11–15, 22]. Stability to β-lactamases increases the activity of ceftriaxone against otherwise resistant Gram-negative bacteria [11–15, 22]. Ceftriaxone has also been investigated for efficacy in preventing relapse to cocaine addiction [15]. Ceftriaxone is often used (in combination, but not directly, with macrolide and/or aminoglycoside antibiotics) for the treatment of community-acquired or mild to moderate health care-associated pneumonia. Ceftriaxone is a choice drug for the treatment of bacterial meningitis [11–15, 22].

The potential applications and physicochemical properties of fullerenes have been investigated. Various empty carbon fullerenes with different "*n*" numbers, such as C_{60}, C_{70}, C_{76}, C_{82} and C_{86}, have been obtained. The chemical, physical and mechanical properties of empty, exo- and endo-hedral fullerenes have been the subject of many studies [23–41]. The compressive mechanical properties of fullerene molecules C_n ($n = 20$, 60, 80 and 180) were investigated and discussed in detail using a quantum

molecular dynamics (QMD) technique [25–41]. The unique stability of molecular allotropes, such as C_{60} and C_{70}, was demonstrated in 1985 [23, 25]. This event led to the discovery of a whole new set of carbon-based substances known as fullerenes.

The electrochemical properties of the C_{60} have been studied when these materials became available in macroscopic quantities [26–31]. In 1990, Haufler et al. [32] demonstrated that CH_2Cl_2 electrochemically reduces C_{60} to C_{60}^{1-} and C_{60}^{2-}. Xie et al. [33] cathodically reduced C_{60} in six reversible one-electron steps for -0.97 V vs. Fc/Fc^+ (Fc = ferrocene). This result, along with the inability to perform anodic electrochemistry on fullerenes, revealed the electronic structure of fullerenes, the LUMO orbitals of C_{60} can accept up to six electrons to form C_{60}^{6-}, but the position of the HOMO orbitals does not allow for hole-doping under the usual reported electrochemical conditions. Jehoulet et al. [34] reported on the irreversible electrochemical and structural reorganization of solid fullerenes in acetonitrile. Janda et al. [35] improved upon the experimental conditions by investigating highly organized C_{60} films on highly oriented pyrolytic graphite in an aqueous medium. The reduction of these films induces a morphological change; they re-structure into conductive nano-clusters of ~ 100 nm in diameter [35, 36].

Graph theory has been a useful tool in assessing the quantitative structural activity relationship and quantitative structural property relationship [42–53]. A lot of studies in different areas have used topological indices [42–50]. Any extrapolation of results from one compound to other compounds must take into account considerations based on a QSAR study, which depends on how close the chemical properties are of the compounds in question. Effective mathematical methods must be employed to make good correlations between several properties of chemicals. Several applications of the indices have been reported [42–53]. The number of carbon atoms in the various fullerene structures was determined with these applications.

The Marcus theory builds on the Arrhenius equation for the rates of chemical reactions in two ways. A formula for the pre-exponential factor in the Arrhenius equation, based on the electronic coupling between the initial and final state of the electron transfer reaction (i.e., the overlap of the electronic wave functions of the two states), is provided. A formula for the activation energy, based on a parameter called the reorganization energy, and the Gibbs free energy is given. Although electrons are commonly described as residing in electron bands in bulk materials and electron orbitals in molecules, the following description will be described in molecular terms. When a photon excites a molecule, an electron in a ground state orbital can be excited to a higher energy orbital. This

excited state leaves a vacancy in a ground state orbital that can be filled by an electron donor. An electron is produced in a high-energy orbital and can be donated to an electron acceptor. Photo-induced electron transfer is an electron transfer that occurs when certain photoactive materials interact with light, including semiconductors that can be photo-activated, such as many solar cells, biological systems like those used in photosynthesis, and small molecules with suitable absorptions and redox states [54–62].

The electron transfer process is one of the most important chemical processes in nature and plays a central role in many biological, physical and chemical systems. Solid-state electronics depends on the control of the electron transfer in semiconductors and the new area of molecular electronics depends critically on the understanding and control of the transfer of electrons between molecules and nanostructures. The other reason to study electron transfer is that it is a simple kind of chemical reaction, and by understanding it, one can gain insight into other kinds of chemistry and biochemistry. After all, what is important is the chemistry of the transfer of electrons from one place to another [55–62].

The free energy of electron transfer ΔG_{et} is the difference between the reactants on the left and the products on the right, and $\Delta G_{et}^{\#}$ is the activation energy [55–62].

The Marcus theory is currently the dominant theory of ET process in chemistry. The Marcus theory has widely accepted because it makes surprising predictions about electron transfer rates that have been supported experimentally over the last several decades. The most significant prediction is that the rate of electron transfer will increase as the electron transfer reaction becomes more exergonic, but only to a point [55–62]. Electron transfer happens in the chemical reactions. Is it any particular model and mechanism that works well in this case in analogy with many such models and mechanisms that work fine in material sciences [63–69].

Here, were calculated the first to fourth activation free energies of electron transfer $\Delta G_{et(n)}^{\#}$ ($n = 1$–4) and the kinetic rate constants of the electron transfers k_{et} ($n = 1$–4) using the Marcus theory and the equations on the basis of the first to fourth reduction potentials ($^{Red.}E_1$–$^{Red.}E_4$) of fullerenes C_n ($n = 60, 70, 76, 82$ and 86) for the predicted supramolecular complexes [cefadroxil]·C_n **7–11** and **37–40**; [cefepime]·C_n, **12–16** and **41–44**; [cephalexin]·C_n, **17–21** and **45–48**; [cefotaxime]·C_n, **22–26** and **49–52**; [cefoperazone]·C_n, **27–31** and **53–56** and [ceftriaxone]·C_n, **32–36** and **57–60** (supramolecular complexes **7–60**). See Eqs. 2 and 3, Tables 6, 7, 8, 9 and 10 and Fig. 3.

This study elaborates upon the relationship between the number of carbon atoms and the four free energies of

electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of fullerenes C_n ($n = 60$, 70, 76, 82 and 86) with cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone on the basis of the four reduction potentials ($^{Red.}E_1$–$^{Red.}E_4$) of the fullerenes.

The relationships are assessed by applying the Rehm-Weller equation [54] to create [cefadroxil]. C_n, **A-1** to **A-5**; [cefepime]·C_n, **B-1** to **B-5**; [cephalexin]·C_n, **C-1** to **C-5**; [cefotaxime]·C_n, **D-1** to **D-5**; [cefoperazone]·C_n, **E-1** to **E-5** and [ceftriaxone]·C_n, **F-1** to **F-5**. The results were extended to calculate the four free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of other supramolecular complexes of cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone as a class of electron-transfers with fullerenes C_{60}–C_{300} ([cephalosporin antibiotics]·C_n complexes: [cefadroxil]·C_n **7–11** and **37–40**; [cefepime]·C_n, **12–16** and **41–44**; [cephalexin]·C_n, **17–21** and **45–48**; [cefotaxime]·C_n, **22–26** and **49–52**; [cefoperazone]·C_n, **27–31** and **53–56** and [ceftriaxone]·C_n, **32–36** and **57–60**, supramolecular complexes **7–121**). This study calculated the four free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of **A-1** to **A-19**, **B-1** to **B-19**, **C-1** to **C-19**, **D-1** to **D-19**, **E-1** to **E-19** and **F-1** to **F-19** (see Eqs. 1–23, Tables 1, 2, 3, 4, 5; Figs. 1, 2).

Also, in this study, were calculated the activate free energies of electron transfer and the maximum wave length of the electron transfers, $\Delta G^{\#}_{et(n)}$ and λ_{et}, respectively, using Marcus theory and the equations on the basis of the oxidation potentials of fullerenes C_n ($n = 60$, 70, 76, 82 and 86) to predict the data of the electron transfer process between the antibiotic compounds (cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone) and the fullerenes.

One of the aspects in this study was the relationship between the number of carbon atoms in the fullerenes C_n (C_{60}, C_{70}, C_{76}, C_{82} and C_{86}) and the data values on the electron transfer (ΔG_{et}, in kcal mol^{-1}) between the antibiotic compounds (cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone) with the fullerenes.

One of the other aspects of this study was the investigation of the photo-electron transfer process to find more medicinal activity conditions and properties for the antibiotics **1–6** in the presence of the selected fullerenes by performing the supramolecular complexes [antibiotics **1–6**]·C_n.

Graphing and mathematical method

For the entire diagram operations were applied Microsoft Office Excel-2003. To investigate several properties of the fullerenes can be utilized the number of carbon atoms of the fullerenes. The values were applied to calculate $\Delta G_{et(1)}$–$\Delta G_{et(4)}$, according to the Rehm-Weller equation for the complexes [cefadroxil]·C_n **7–11** and **37–40**; [cefepime]·C_n, **12–16** and **41–44**; [cephalexin]·C_n, **17–21** and **45–48**; [cefotaxime]·C_n, **22–26** and **49–52**; [cefoperazone]·C_n, **27–31** and **53–56** and [ceftriaxone]·C_n, **32–36** and **57–60** (supramolecular complexes **7–60**).

The linear multiple linear regressions and nonlinear models have utilized in this study. The Eqs. 1 and 4–23 were applied to calculate the values of $\Delta G_{et(1)}$–$\Delta G_{et(4)}$ for complexes that have not been reported in the literature. The best results and equations to extend the physicochemical data have chosen [48, 53].

Table 1 The data values on the Cefadroxil **1** and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol^{-1}, between Cefadroxil and C_n (as [Cefadroxil].C_n; **7–11** and **37–40**) supramolecular complexes

No.	Row	Formula of [Cefadroxil]·C_n	(ΔG_{et}) in kcal mol^{-1} [Cefadroxil]·C_n			
			$\Delta G_{et(1)}$	$\Delta G_{et(2)}$	$\Delta G_{et(3)}$	$\Delta G_{et(4)}$
7	A-1	[Cefadroxil].C_{60}	51.70	60.80	71.08	81.71
8	A-2	[Cefadroxil].C_{70}	50.35	59.40	67.93	77.80
9	A-3	[Cefadroxil].C_{76}	47.28	55.87	65.79	75.09
10	A-4	[Cefadroxil].C_{82}	42.53	50.33	63.48	72.11
11	A-5	[Cefadroxil].C_{86}	38.41	45.51	61.84	69.96
37	A-6	[Cefadroxil].C_{78}	45.89	54.25	65.04	74.13
38	A-7	[Cefadroxil].C_{84}	40.56	48.03	62.67	71.05
39	A-8	[Cefadroxil].C_{96}	24.84	29.55	57.38	64.07
40	A-9	[Cefadroxil].C_{120}	−26.90	−31.60	44.61	46.81

The data of $\Delta G_{et(n)}$ ($n = 1$–4) were predicted by using Eqs. 4–7, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

The data of the free energy of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) for [Cefadroxil]·C_n compounds had not been previously reported

Table 2 The data values on the Cefepime **2** and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol^{-1}, between Cefepime with C_n (as [Cefepime]·C_n, **12-16** and **41-44**) supramolecular complexes

No.	Row	Formula of [Cefepime]·C_n	(ΔG_{et}) in kcal mol^{-1} [Cefepime]·C_n			
			$\Delta G_{et(1)}$	$\Delta G_{et(2)}$	$\Delta G_{et(3)}$	$\Delta G_{et(4)}$
12	B-1	[Cefepime].C$_{60}$	50.80	59.90	70.18	80.81
13	B-2	[Cefepime].C$_{70}$	49.45	58.50	67.03	76.90
14	B-3	[Cefepime].C$_{76}$	46.38	54.97	64.89	74.19
15	B-4	[Cefepime].C$_{82}$	41.63	49.43	62.58	71.21
16	B-5	[Cefepime].C$_{86}$	37.51	44.61	60.94	69.06
41	B-6	[Cefepime].C$_{78}$	44.99	53.35	64.14	73.23
42	B-7	[Cefepime].C$_{84}$	39.66	47.13	61.77	70.15
43	B-8	[Cefepime].C$_{96}$	23.94	28.65	56.48	63.17
44	B-9	[Cefepime].C$_{120}$	−27.80	−32.50	43.71	45.91

The data of $\Delta G_{et(n)}$ ($n = 1–4$) were predicted by using Eqs. 8–11, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

The data of the free energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) for [Cefepime]·C_n compounds had not been previously reported

Table 3 The data values on the Cephalexin **3** and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol^{-1}, between Cephalexin with C_n (as [Cephalexin]·C_n, **17–21** and **45–48**) supramolecular complexes

No.	Row	Formula of [Cephalexin]·C_n	(ΔG_{et}) in kcal mol^{-1} [Cephalexin]·C_n			
			$\Delta G_{et(1)}$	$\Delta G_{et(2)}$	$\Delta G_{et(3)}$	$\Delta G_{et(4)}$
17	C-1	[Cephalexin].C$_{60}$	38.90	47.14	57.96	68.61
18	C-2	[Cephalexin].C$_{70}$	37.35	45.61	54.82	64.70
19	C-3	[Cephalexin].C$_{76}$	34.26	41.99	52.69	61.99
20	C-4	[Cephalexin].C$_{82}$	29.55	36.36	50.37	59.01
21	C-5	[Cephalexin].C$_{86}$	25.51	31.47	48.72	56.86
45	C-6	[Cephalexin].C$_{78}$	32.87	40.34	51.94	61.03
46	C-7	[Cephalexin].C$_{84}$	27.62	34.03	49.56	57.95
47	C-8	[Cephalexin].C$_{96}$	12.26	15.33	44.23	50.97
48	C-9	[Cephalexin].C$_{120}$	−37.90	−46.34	31.32	33.71

The data of $\Delta G_{et(n)}$ ($n = 1–4$) were predicted by using Eqs. 12–15, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

The data of the free energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) for [Cephalexin]·C_n compounds had not been previously reported

The free energy changes between an electron donor (D) and an acceptor (A) for the electron transfer (ET) were estimates by the Rehm-Weller equation:

$$\Delta G^o = e[E_D^o - E_A^o] - \Delta E^* + \omega_1 \qquad (1)$$

In this equation, "e" is the unit electrical charge. The reduction potentials of the electron donor and acceptor were introduced as E_D^0 and E_A^0, respectively. The value of ΔE^* is the energy of the singlet or triplet excited state. The work required to bring the donor and acceptor to within the electron transfer (ET) distance has determined by ω_1. The work term in this expression is zero if an electrostatic complex forms before the ET-process [54].

The Marcus theory of ET-process suggests rather weak electronic coupling between the initial (LE) and final (ET), locally excited and electron transfer states, respectively.

The transition state (TS) is near to the crossing point of the LE and ET terms. The value of the ET rate constant is controlled by the $\Delta G_{et}^{\#}$, which is a function of the reorganization energy (RE; l/4) and the ET driving force, ΔG_{et}:

$$\Delta G_{et}^{\#} = (l/4)(1 + \Delta G_{et}/l)^2, \qquad (2)$$

The reorganization energy (RE) has defined as the energy required reorganizing the system structure from the initial to final coordinates without changing the electronic state. The RE was found to be in the range 0.1–0.3 eV for organic molecules. Here, the minimum amount of RE was used [55–62].

The Planck's formula has applied to calculate the maximum wavelengths ($\lambda_{(n)}$) of the electromagnetic photon for the ET-process in the selected nanostructure complexes:

Table 4 The data values on the Dodecahydro Cefotaxime **4** and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol^{-1}, between Cefotaxime with C_n (as [Cefotaxime]·C_n, **22-26** and **49-52**) supramolecular complexes

No.	Row	Formula of [Cefotaxime]·C_n	(ΔG_{et}) in kcal mol^{-1} [Cefotaxime]·C_n			
			$\Delta G_{et(1)}$	$\Delta G_{et(2)}$	$\Delta G_{et(3)}$	$\Delta G_{et(4)}$
22	D-1	[Cefotaxime].C_{60}	48.80	57.80	68.09	78.70
23	D-2	[Cefotaxime].C_{70}	47.45	56.40	64.93	74.81
24	D-3	[Cefotaxime].C_{76}	44.38	52.87	62.80	72.10
25	D-4	[Cefotaxime].C_{82}	39.63	47.33	60.48	69.11
26	D-5	[Cefotaxime].C_{86}	35.51	42.51	58.84	66.97
49	D-6	[Cefotaxime].C_{78}	42.99	51.25	62.05	71.13
50	D-7	[Cefotaxime].C_{84}	37.66	45.03	59.67	68.06
51	D-8	[Cefotaxime].C_{96}	21.94	26.55	54.38	61.07
52	D-9	[Cefotaxime].C_{120}	−29.80	−34.60	68.09	43.78

The data of $\Delta G_{et(n)}$ (n = 1–4) were predicted by using Eqs. 16–19, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

The data of the free energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) for [Cefotaxime]·C_n compounds had not been previously reported

Table 5 The data values on the CFO **5** and ROC **6** and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol^{-1}, between CFO and ROC with C_n (as [CFO]·C_n, **27–31** and **53–56** and [ROC]·C_n, **32–36** and **57–60**) supramolecular complexes

No.	Row	Formula of [CFO]·C_n	No.	Row	Formula of [ROC]·C_n	(ΔG_{et}) in kcal mol^{-1} [CFO and ROC]·C_n			
						$\Delta G_{et(1)}$	$\Delta G_{et(2)}$	$\Delta G_{et(3)}$	$\Delta G_{et(4)}$
27	E-1	[CFO].C_{60}	32	F-1	[ROC].C_{60}	49.50	58.04	68.76	79.41
28	E-2	[CFO].C_{70}	33	F-2	[ROC].C_{70}	48.15	56.51	65.60	75.50
29	E-3	[CFO].C_{76}	34	F-3	[ROC].C_{76}	45.08	52.89	63.47	72.79
30	E-4	[CFO].C_{82}	35	F-4	[ROC].C_{82}	40.33	47.26	61.16	69.81
31	E-5	[CFO].C_{86}	36	F-5	[ROC].C_{86}	36.21	42.37	59.52	67.66
53	E-6	[CFO].C_{78}	57	F-6	[ROC].C_{78}	43.69	51.24	62.72	71.83
54	E-7	[CFO].C_{84}	58	F-7	[ROC].C_{84}	38.36	44.93	60.35	68.75
55	E-8	[CFO].C_{96}	59	F-8	[ROC].C_{96}	22.64	26.23	55.08	61.77
56	E-9	[CFO].C_{120}	60	F-9	[ROC].C_{120}	−29.10	−35.44	42.41	44.51

The data of the free energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) for [CFO]·C_n and [ROC]·C_n compounds had not been previously reported

The data of $\Delta G_{et(n)}$ (n = 1–4) were predicted by using Eqs. 4–7, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

$$\Delta G_{et}^{\#} = \Delta E = h \times c/\lambda_{(n)}. \tag{3}$$

In this study, has also used this formula to calculate the activation free energy of the ET-process [63, 69, 70].

Discussion

Cefadroxil is a first-generation cephalosporin and is effective against Gram-positive cocci. In 2000, the electro-oxidation of cefadroxil was investigated by Özkan et al. [71], and they used a glassy carbon electrode (GCE) for cyclic voltammetry (CV) and differential pulse voltammetry (DPV)

Cefepime was studied by electrochemical reduction and oxidation with a carbon electrode in an aqueous buffer solution of pH < 8.0 [72]. Electro-analysis of cefalexin was performed in a 0.1 M carbonate buffer (pH 9.2) using a boron-doped diamond thin-film electrodes for CV measurements [73].

Cefalexin was measured polarographically in pure form and in pharmaceutical preparations based on the catalytic hydrogen wave observed in the presence of cobalt (II) and the drug at a potential of −1.47 V versus SCE [51]. The electro-oxidation of cefalexin at boron-doped diamond electrodes and glassy carbon electrodes was investigated by CV [75].

In 2009, the electrochemical behavior of cefotaxime was studied using modified carbon paste electrode (Nigam et al. [14]). CV and DPV were used for the estimation of the drug using a modified carbon paste capillary as the working electrode [53]. Voltammograms

Antibiotics 1-6
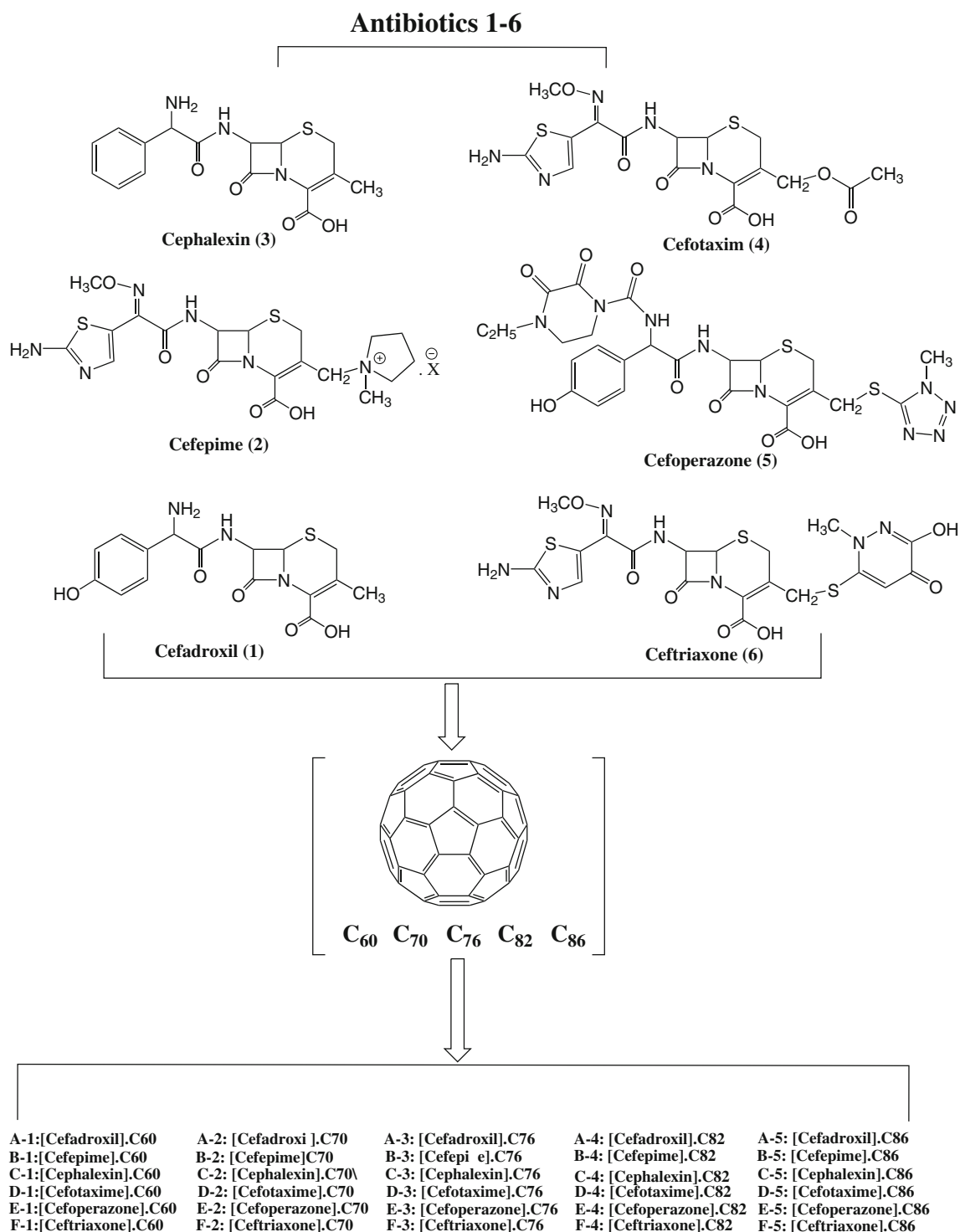
Fig. 1 The conjectured structures of cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone (CFO) and ceftriaxone (ROC) as well as the fullerenes C_n ($n = 60$, 70, 76, 82 and 86), which create [cefadroxil]·C_n **A-1** to **A-5**; [cefepime]·C_n, **B-1** to **B-5**; [cephalexin]·C_n, **C-1** to **C-5**; [cefotaxime]·C_n, **D-1** to **D-5**; [cefoperazone]·C_n, **E-1** to **E-5** and [ceftriaxone]·C_n, **F-1** to **F-5**

were recorded in a potential window—0.2–1.1 V vs. Ag/AgCl at various scan rates and DPV with a pulse width 0.05 s [76].

Various concentrations of cefotaxime from 0.1 mM to 1 nM were analyzed in water and in acidified human blood samples (pH 2.3) [76].
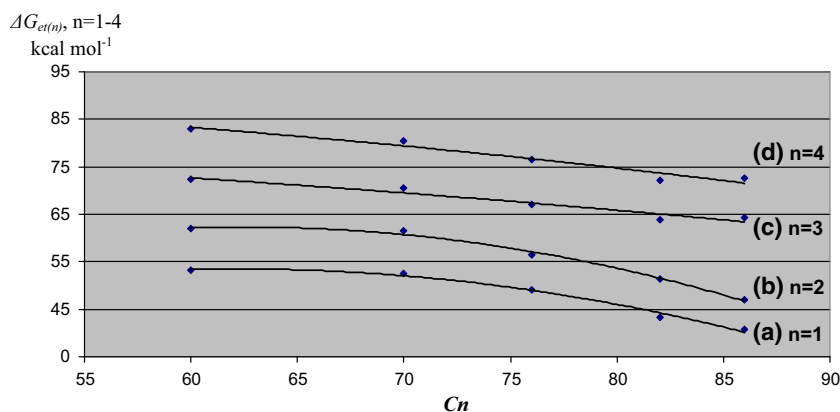
Fig. 2 The relationship between the number of carbon atoms "n" of the fullerenes and the first (**a**) to fourth (**d**) of ($\Delta G_{et(n)}$, $n = 1$–4) in ET-process of [Cefadroxil]·C_n ($n = 60$, 70, 76, 82 and 86), compounds **A-1** to **A-5** (**7–11**). *Asterisk* the related curves for

[Cefepime]·C_n, **B-1** to **B-5**, [Cephalexin]·C_n, **C-1** to **C-5**, [Cefotaxime]@C_n, **D-1** to **D-5** Cefoperazone]·C_n, **E-1** to **E-5** and [Ceftriaxone]·C_n, **F-1** to **F-5** have similar style to Fig. 2(**a–d**) [Cefadroxil]·C_n **A-1** to **A-5**

Two cephalosporin antibiotic derivatives, cefoperazone and ceftriaxone, were studied with direct current, differential pulse polarography (DPP) and CV methods [77]. The electro-oxidation of both cephalosporin derivatives had studied at the carbon paste electrode (CPE). Both drugs gave rise to one oxidation peak at about +1.05 V vs. SCE [77].

The oxidation potentials of cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone, which have been previously reported [71–78] are as follows:

No.	Cephalosporin derivatives	Oxidation potential (^{Ox}E, in volts)	Reference number
1	Cefadroxil	+1.15	[71]
2	Cefepime	+0.97	[72, 73]
3	Cephalexin	+0.58	[74, 75]
4	Cefotaxime	+1.02	[76]
5	Cefoperazone	+1.05	[77]
6	Ceftriaxone	+1.05	[77]

The four reported reduction potentials ($^{Red.}E_1$–$^{Red.}E_4$) of fullerenes C_n are as follows. For C_{60}, the potentials $^{Red.}E_1$–$^{Red.}E_4$ are -1.12, -1.50, -1.95 and -2.41 V, respectively [79]. The $^{Red}E_n$ ($n = 1$–4) for C_{70} are -1.09, -1.48, -1.87 and -2.30 V, respectively [79]. The values of $^{Red}E_n$ ($n = 1$–4) for C_{76} are -0.94, -1.26, -1.72 and -2.13 V, respectively [79]. The values of $^{Red}E_n$ ($n = 1$–4) for C_{82} are -0.69, -1.04, -1.58 and -1.94 V, respectively [79]. The $^{Red}E_n$ ($n = 1$–4) for C_{86} are -0.58, -0.85, -1.60 and -1.96 V, respectively [79]. C_{180} and C_{240} were not prepared or isolated along with the fullerenes have listed in Tables 1, 2, 3, 4.

Tables 1, 2, 3, 4 and 5 contain a summary of the data. The calculated values for **6–1** of the four electron transfer free energies ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$, in kcal mol^{-1}) between the cephalosporin antibiotics **1–5** and fullerenes C_n ($n = 60$, 70, 76, 82 and 86) as [cephalosporin antibiotics]·C_n complexes are shown. These values were calculated using the Rehm-Weller equation (Eq. 1). The selected cephalosporin antibiotics (**1–5**) were used to model the structural relationship between the number of carbon atoms (n) in the selected fullerenes and $\Delta G_{et(n)}$ ($n = 1$–4). The data of compounds [cefadroxil]·C_n, **A-1** to **A-19**; [cefepime]·C_n, **B-1** to **B-19**; [cephalexin]·C_n, **C-1** to **C-19**; [cefotaxime]·C_n, **D-1** to **D-19**; [cefoperazone]·C_n, **E-1** to **E-19** and [ceftriaxone]·C_n, **F-1** to **F-19** (complexes **7–60**) are reported in the appropriate tables. Figure 1 depicts the structures of cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone as well as fullerenes C_n ($n = 60$, 70, 76, 82 and 86). The fullerenes and cephalosporin antibiotics were combined to create [cefadroxil]·C_n, **A-1** to **A-5**; [cefepime]·C_n, **B-1** to **B-5**; [cephalexin]·C_n, **C-1** to **C-5**; [cefotaxime]·C_n, **D-1** to **D-5**; [cefoperazone]·C_n, **E-1** to **E-5** and [ceftriaxone]·C_n, **F-1** to **F-5**.

Figures 2a, d have shown the relationships between the number of carbon atoms (n) in the fullerenes and the first to fourth free-energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of [cefadroxil]·C_n ($n = 60$, 70, 76, 82 and 86). Equations 4–7 correspond to Fig. 2a, d. This data were fitted with a second-order polynomial equation. The R-squared values (R^2) for these graphs are 0.9875, 0.9923, 0.9384 and 0.9478, respectively.

Equations 4–7 can be utilized to calculate the values of $\Delta G_{et(1)}$–$\Delta G_{et(4)}$ of [cefadroxil]·C_n. Table 1 contains the calculated values of the free energies of electron transfer ($\Delta G_{et(n)}$, $n = 1$–4) between the selected cefadroxil and C_n (as [cefadroxil]·C_n compounds **A-1** to **A-5**) **7–11**

supramolecular complexes. The $\Delta G_{et(n)}$ ($n = 1$–4) for [cefadroxil]·C_n (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}) are predicted using Eqs. 4–7 and the Rehm-Weller equation (see Table 1).

Equations 8–11 have shown the relationships between the number of carbon atoms in the fullerenes and the first to fourth free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of [cefepime]·C_n (n = selected fullerenes). These data were fitted with a second-order polynomial equation. The R^2 values for these graphs are 0.9875, 0.9924, 0.9384 and 0.9478, respectively.

Using Eqs. 1 and 8–11, the $\Delta G_{et(1)}$–$\Delta G_{et(4)}$ values of [cefepime]·C_n can be calculated. Table 2 involves the calculated values of the free energies of electron transfer ($\Delta G_{et(n)}$, $n = 1$–4) between cefepime and the C_n (as [cefepime]·C_n compounds **B-1** to **B-5**) **12–16** supramolecular complexes. The $\Delta G_{et(n)}$ ($n = 1$–4) for [cefepime]·C_n (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}) have predicted using Eqs. 8–11 and the Rehm-Weller equation (see Table 2).

The results of Rehm-Weller equation have demonstrated the free energies of electron transfer ($\Delta G_{et(n)}$, $n = 1$–4) between cephalexin and the selected fullerenes. Equations 12–15 have shown the relationships between the number of carbon atoms of the fullerenes and the first to fourth free energies of electron transfer of [cephalexin]·C_n ($n = 60, 70, 76, 82$ and 86). These data were fit with a second-order polynomial. The R^2 values for these graphs are 0.9885, 0.9924, 0.9387 and 0.9478, respectively.

Using Eqs. 12–15, the values of $\Delta G_{et(1)}$–$\Delta G_{et(4)}$ of [cephalexin]·C_n can be calculated. Table 3 contains the calculated values of the free energies of electron transfer ($\Delta G_{et(n)}$, $n = 1$–4) between the cephalexin and the fullerenes (as [Cephalexin]·C_n **C-1** to **C-5**) **17–21** supramolecular complexes. The $\Delta G_{et(n)}$ ($n = 1$–4) for [cephalexin]·C_n (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}) are predicted using Eqs. 12–15 and the Rehm-Weller equation (see Table 3).

Equations 16–19 have shown the relationships between the number of carbon atoms in the selected fullerenes and the $\Delta G_{et(1)}$–$\Delta G_{et(4)}$ values of [cefotaxime]·C_n (n = selected fullerenes). These data were fitted with a second-order polynomial equation. The R^2 values for these graphs are 0.9876, 0.9923, 0.9386 and 0.9476, respectively.

Using Eqs. 1 and 16–19, the values of $\Delta G_{et(1)}$–$\Delta G_{et(4)}$ of [cefotaxime]·C_n can be calculated. Table 4 contains the 76 calculated values of the free energies of electron transfer ($\Delta G_{et(n)}$, $n = 1$–4) between the cefotaxime and the fullerenes (as [cefotaxime]·C_n, compounds **D-1** to **D-5**) **22–26** supramolecular complexes. The $\Delta G_{et(n)}$ ($n = 1$–4) for [cefotaxime]·C_n (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}) are predicted using Eqs. 16–19 and the Rehm-Weller equation (see Table 4).

Equations 20–23 demonstrate the relationships between the number of carbon atoms in the fullerenes and the first, second, third and fourth free-energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of [cefoperazone]·C_n and [ceftriaxone]·C_n ($n = 60, 70, 76, 82$ and 86). These data were fitted with a second-order polynomial equation. The R^2 values for these graphs are: 0.9874, 0.9924, 0.9386 and 0.9478, respectively.

Using Eqs. 1 and 20–23, the values of $\Delta G_{et(1)}$ to $\Delta G_{et(4)}$ of [Cefoperazone]·C_n and [Ceftriaxone]·C_n can be calculated. Table 5 contains the calculated values of the free energies of electron transfer ($\Delta G_{et(n)}$, $n = 1$–4) between cefoperazone and ceftriaxone with the fullerenes (as [cefoperazone]·C_n compounds **E-1** to **E-5** and [ceftriaxone]·C_n compounds **F-1** to **F-5**) **27–31** and **32–36** complexes, respectively. The $\Delta G_{et(n)}$ ($n = 1$–4) for [cefoperazone]·C_n and [ceftriaxone]·C_n (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}) are predicted using Eqs. 8–11 and the Rehm-Weller equation (see Table 5).

Equations 4–23

Equation No.	$\Delta G_{et(n)} = a(n)^2 + b(n) + c$
4	$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9201(n) - 38.8596$
5	$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4983(n) - 48.3526$
6	$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0125(n) + 79.4105$
7	$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1064(n) + 89.1088$
8	$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9201(n) - 39.7796$
9	$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4988(n) - 49.3125$
10	$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0125(n) + 78.4905$
11	$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1064(n) + 88.1888$
12	$\Delta G_{et(1)} = -0.0225(n)^2 + 2.7732(n) - 46.2585$
13	$\Delta G_{et(2)} = -0.0281(n)^2 + 3.5028(n) - 61.6624$
14	$\Delta G_{et(3)} = -0.0026(n)^2 + 0.0259(n) + 65.7913$
15	$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1064(n) + 75.9688$
16	$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9197(n) - 41.8287$
17	$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4983(n) - 51.3526$
18	$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0076(n) + 76.6012$
19	$\Delta G_{et(4)} = -0.0039(n)^2 + 0.1112(n) + 85.9282$
20	$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9196(n) - 41.1378$
21	$\Delta G_{et(2)} = -0.0281(n)^2 + 3.5028(n) - 50.8224$
22	$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0036(n) + 77.4210$
23	$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1064(n) + 86.8088$

By application of these results (Eqs. 4–23) and the Rehm-Weller equation, the electron transfer energies ($\Delta G_{et(n)}$, $n = 1$–4) of the complexes formed by the selected cephalosporin antibiotics and fullerenes (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}) were approximated. The calculated values of the free electron transfer energies ($\Delta G_{et(n)}$,

$n = 1$–4) for the selected [cephalosporin antibiotics **1–6**]·C_n ($n = 60, 70, 76, 82$ and 86, compounds **7–60**) are shown in Tables 1, 2, 3, 4 and 5. The calculated and the predicted values agreed with good approximation. In lieu of increasing the number of carbons atoms (n) in the selected fullerene structures, the values of $\Delta G_{et(n)}$ ($n = 1$–4) have decreased. Electron transfer (ET) appears to increase with the electron population in the C_n structures (see Tables 1, 2, 3, 4, 5). These results may be related to the HOMO–LUMO gaps of the fullerenes. The tables have also shown that some of the $\Delta G_{et(n)}$ ($n = 1$–4) values of the complexes are negative.

Tables 6, 7, 8, 9 and 10 show the calculated values of the first to fourth free activation energies of electron transfer and the kinetic rate constants of the electron transfers by utilizing Eqs. 2 and 3 for **7–60** in accordance with the Marcus theory. Figure 3 shows the surfaces of the free energies of electron transfer between cefadroxil, cefepime, cephalexin, cefotaxime and cefoperazone and

ceftriaxone and the fullerenes ($n = 60, 70, 76, 82$ and 86). The values of the first to fourth activated free energies of electron transfer for **7–60** increase with increasing $\Delta G_{et(n)}$ and the number of carbon atoms in the complexes, while the kinetic rate constants of electron transfer decrease with increasing $\Delta G_{et(n)}$ and $\Delta G_{et(n)}^{\#}$ ($n = 1$–4) for **7–60**. The zero values mean that there was not any electron transfer process between those parts of the predicted complexes (see Tables 6, 7, 8, 9, 10; Fig. 3).

By using Eq. 1 (Rehm-Weller equation), Eqs. 2 and 3 (Marcus theory) and Eqs. 4–23, the values of $\Delta G_{et(n)}$ ($n = 1$–4), $\Delta G_{et(n)}^{\#}$ and $\lambda_{(n)}$ ($n = 1$–4) were calculated for **7–60**. The values of the number of carbon atoms (n) show a good relationship with $\Delta G_{et(n)}$ ($n = 1$–4), $\Delta G_{et(n)}^{\#}$ and $k_{et(n)}$ ($n = 1$–4) for all of the cephalosporin-fullerene complexes. Figure 3 shows the surfaces of the free energies of electron transfer $\Delta G_{et(n)}$ and $\Delta G_{et(n)}^{\#}$ ($n = 1$–4) between **1** and **5** and the fullerenes ($C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84}$ and C_{120})

Table 6 The values of the first to forth free activation energies of electron transfer and the wavelengths of the photoelectron transfer process, $\Delta G_{et(n)}^{\#}$ (in kcal mol^{-1}, n-1-4) and $\lambda_{et(n)}$ (nm, $n = 1$–4), respectively, of [Cefadroxil]·C_n supramolecular complexes (**7–11** and **37–40**) supramolecular complexes

Id.	[Cefadroxil]·C_n	$\Delta G_{et(1)}^{\#}$	$\lambda_{et(1)}$	$\Delta G_{et(2)}^{\#}$	$\lambda_{et(2)}$	$\Delta G_{et(3)}^{\#}$	$\lambda_{et(3)}$	$\Delta G_{et(4)}^{\#}$	$\lambda_{et(4)}$
7	[Cefadroxil].C_{60}	100.43	285	131.46	217	173.52	165	222.59	128
8	[Cefadroxil].C_{70}	98.17	291	129.73	220	165.63	173	210.29	136
9	[Cefadroxil].C_{76}	87.21	328	111.38	257	151.3	189	191.99	149
10	[Cefadroxil].C_{82}	70.4	406	94.46	303	138.5	206	172.53	166
11	[Cefadroxil].C_{86}	63.55	450	80.96	353	140.28	204	174.52	164
37	[Cefadroxil].C_{78}	82.33	347	109.19	262	149.49	191	188.31	152
38	[Cefadroxil].C_{84}	67.18	426	88.85	322	140.09	204	174.65	164
39	[Cefadroxil].C_{96}	31.45	909	40.75	702	120.23	238	145.60	196
40	[Cefadroxil].C_{120}	8.47	3,376	13.57	2,107	78.55	364	85.11	336

The data of $\Delta G_{et(n)}^{\#}$ (in kcal mol^{-1}, n-1-4) and λ_{et} (s^{-1}, $n = 1$–4) for [Cefadroxil]·C_n supramolecular complexes (**7–11** and **37–40**)

Table 7 The values of the first to forth free activation energies of electron transfer the wavelengths of the photoelectron transfer process, $\Delta G_{et(n)}^{\#}$ (in kcal mol^{-1}, n-1-4) and $\lambda_{et(n)}$ (nm, $n = 1$–4), respectively, of [Cefepime]·C_n supramolecular complexes (**12–16** and **41–44**) supramolecular complexes

Id.	[Cefepime]·C_n	$\Delta G_{et(1)}^{\#}$	$\lambda_{et(1)}$	$\Delta G_{et(2)}^{\#}$	$\lambda_{et(2)}$	$\Delta G_{et(3)}^{\#}$	$\lambda_{et(3)}$	$\Delta G_{et(4)}^{\#}$	$\lambda_{et(4)}$
12	[Cefepime].C_{60}	97.42	293	127.97	223	169.55	169	218.09	131
13	[Cefepime].C_{70}	95.19	300	126.26	226	161.76	177	205.92	139
14	[Cefepime].C_{76}	84.4	339	108.2	264	147.59	194	187.81	152
15	[Cefepime].C_{82}	67.88	421	91.53	312	134.95	212	168.57	170
16	[Cefepime].C_{86}	61.16	467	78.26	365	136.72	209	170.54	168
41	[Cefepime].C_{78}	79.66	359	106.12	269	145.88	196	184.27	155
42	[Cefepime].C_{84}	64.77	441	86.07	332	136.6	209	170.76	167
43	[Cefepime].C_{96}	29.81	959	38.88	735	117	244	142.04	201
44	[Cefepime].C_{120}	9.35	3,058	14.68	1,948	75.94	377	82.39	347

The data of $\Delta G_{et(n)}^{\#}$ (in kcal mol^{-1}, n-1-4) and λ_{et} (s^{-1}, $n = 1$–4) for [Cefepime]·C_n supramolecular complexes (**12–16** and **41–44**)

Table 8 The values of the first to forth free activation energies of electron transfer and the wavelengths of the photoelectron transfer process, $\Delta G^{\#}_{et(n)}$ (in kcal mol^{-1}, n-1-4) and $\lambda_{et(n)}$ (nm, $n = 1$–4), respectively, of [Cephalexin]·C$_n$ supramolecular complexes (**17–21** and **45–48**) supramolecular complexes

Id.	[Cephalexin]·C$_n$	$\Delta G^{\#}_{et(1)}$	$\lambda_{et(1)}$	$\Delta G^{\#}_{et(2)}$	$\lambda_{et(2)}$	$\Delta G^{\#}_{et(3)}$	$\lambda_{et(3)}$	$\Delta G^{\#}_{et(4)}$	$\lambda_{et(4)}$
17	[Cephalexin].C$_{60}$	62.53	457	86.5	331	121.21	236	162.72	176
18	[Cephalexin].C$_{70}$	59.98	477	85.1	336	114.63	249	152.23	188
19	[Cephalexin].C$_{76}$	51.48	555	70.4	406	102.86	278	136.72	209
20	[Cephalexin].C$_{82}$	38.75	738	57.06	501	92.26	310	120.38	238
21	[Cephalexin].C$_{86}$	33.74	847	46.69	612	93.72	305	122.04	234
45	[Cephalexin].C$_{78}$	48.02	595	66.58	429	101.39	282	133.77	214
46	[Cephalexin].C$_{84}$	36.79	777	50.71	564	93.66	305	122.3	234
47	[Cephalexin].C$_{96}$	12.51	2,285	16.34	1,750	77.44	369	98.20	291
48	[Cephalexin].C$_{120}$	22.29	1,283	37.34	766	44.56	641	49.96	572

The data of $\Delta G^{\#}_{et(n)}$ (in kcal mol^{-1}, n-1-4) and λ_{et} (s^{-1}, $n = 1$–4) for [Cephalexin]·C$_n$ supramolecular complexes (**17–21** and **65–78**)

Table 9 The values of the first to forth free activation energies of electron transfer and the wavelengths of the photoelectron transfer process, $\Delta G^{\#}_{et(n)}$ (in kcal mol^{-1}, n-1-4) and $\lambda_{et(n)}$ (nm, $n = 1$–4), respectively, of [Cefotaxime]·C$_n$ supramolecular complexes (**22–26** and **49–52**) supramolecular complexes

Id.	[Cefotaxime]·C$_n$	$\Delta G^{\#}_{et(1)}$	$\lambda_{et(1)}$	$\Delta G^{\#}_{et(2)}$	$\lambda_{et(2)}$	$\Delta G^{\#}_{et(3)}$	$\lambda_{et(3)}$	$\Delta G^{\#}_{et(4)}$	$\lambda_{et(4)}$
22	[Cefotaxime].C$_{60}$	90.81	315	120.38	238	160.8	178	208.1	137
23	[Cefotaxime].C$_{70}$	88.63	323	118.72	241	153.16	187	196.25	146
24	[Cefotaxime].C$_{76}$	78.26	365	101.2	283	139.39	205	178.59	160
25	[Cefotaxime].C$_{82}$	62.35	459	85.1	336	127.12	225	159.84	179
26	[Cefotaxime].C$_{86}$	55.92	511	72.32	395	128.83	222	161.76	177
49	[Cefotaxime].C$_{78}$	73.88	387	99.11	288	137.66	208	175.02	163
50	[Cefotaxime].C$_{84}$	59.59	480	79.78	358	128.65	222	161.87	177
51	[Cefotaxime].C$_{96}$	26.32	1,086	34.69	824	109.65	261	133.92	213
52	[Cefotaxime].C$_{120}$	11.47	2,493	17.45	1,638	70.18	407	76.14	376

The data of $\Delta G^{\#}_{et(n)}$ (in kcal mol^{-1}, n-1-4) and λ_{et} (s^{-1}, $n = 1$–4) for [Cefotaxime]·C$_n$ supramolecular complexes (**22–26** and **49–52**)

Table 10 The values of the first to forth free activation energies of electron transfer and the wavelengths of the photoelectron transfer process, $\Delta G^{\#}_{et(n)}$ (in kcal mol^{-1}, n-1-4) and $\lambda_{et(n)}$ (nm, $n = 1$–4), respectively, of Cefoperazone]·C$_n$ (**27–31** and **53–56**) and [Ceftriaxone]·C$_n$, (**32–36** and **57–60**) supramolecular complexes

Id.	[CFO]·C$_n$	Id.	[ROC]·C$_n$	$\Delta G^{\#}_{et(1)}$	$\lambda_{et(1)}$	$\Delta G^{\#}_{et(2)}$	$\lambda_{et(2)}$	$\Delta G^{\#}_{et(3)}$	$\lambda_{et(3)}$	$\Delta G^{\#}_{et(4)}$	$\lambda_{et(4)}$
27	[CFO].C$_{60}$	32	[ROC].C$_{60}$	92.99	307	122.88	233	163.69	175	211.44	135
28	[CFO].C$_{70}$	33	[ROC].C$_{70}$	90.81	315	121.21	236	155.99	183	199.45	143
29	[CFO].C$_{76}$	34	[ROC].C$_{76}$	80.28	356	103.53	276	142.08	201	181.64	157
30	[CFO].C$_{82}$	35	[ROC].C$_{82}$	64.16	446	87.21	328	129.73	220	162.72	176
31	[CFO].C$_{86}$	36	[ROC].C$_{86}$	57.66	496	74.26	385	131.46	217	164.66	174
53	[CFO].C$_{78}$	57	[ROC].C$_{78}$	75.89	377	99.09	289	140.28	204	178.05	161
54	[CFO].C$_{84}$	58	[ROC].C$_{84}$	61.38	466	79.48	360	131.19	218	164.79	174
55	[CFO].C$_{96}$	59	[ROC].C$_{96}$	27.52	1,039	34.07	839	112.07	255	136.60	209
56	[CFO].C$_{120}$	60	[ROC].C$_{120}$	10.71	2,670	18.63	1,535	72.27	396	78.26	365

The data of $\Delta G^{\#}_{et(n)}$ (in kcal mol^{-1}, n-1-4) and λ_{et} (s^{-1}, $n = 1$–4) for Cefoperazone]·C$_n$ (**27–31** and **53–56**) and [Ceftriaxone]·C$_n$, (**32–36** and **57–60**) supramolecular complexes. The data of them are equal
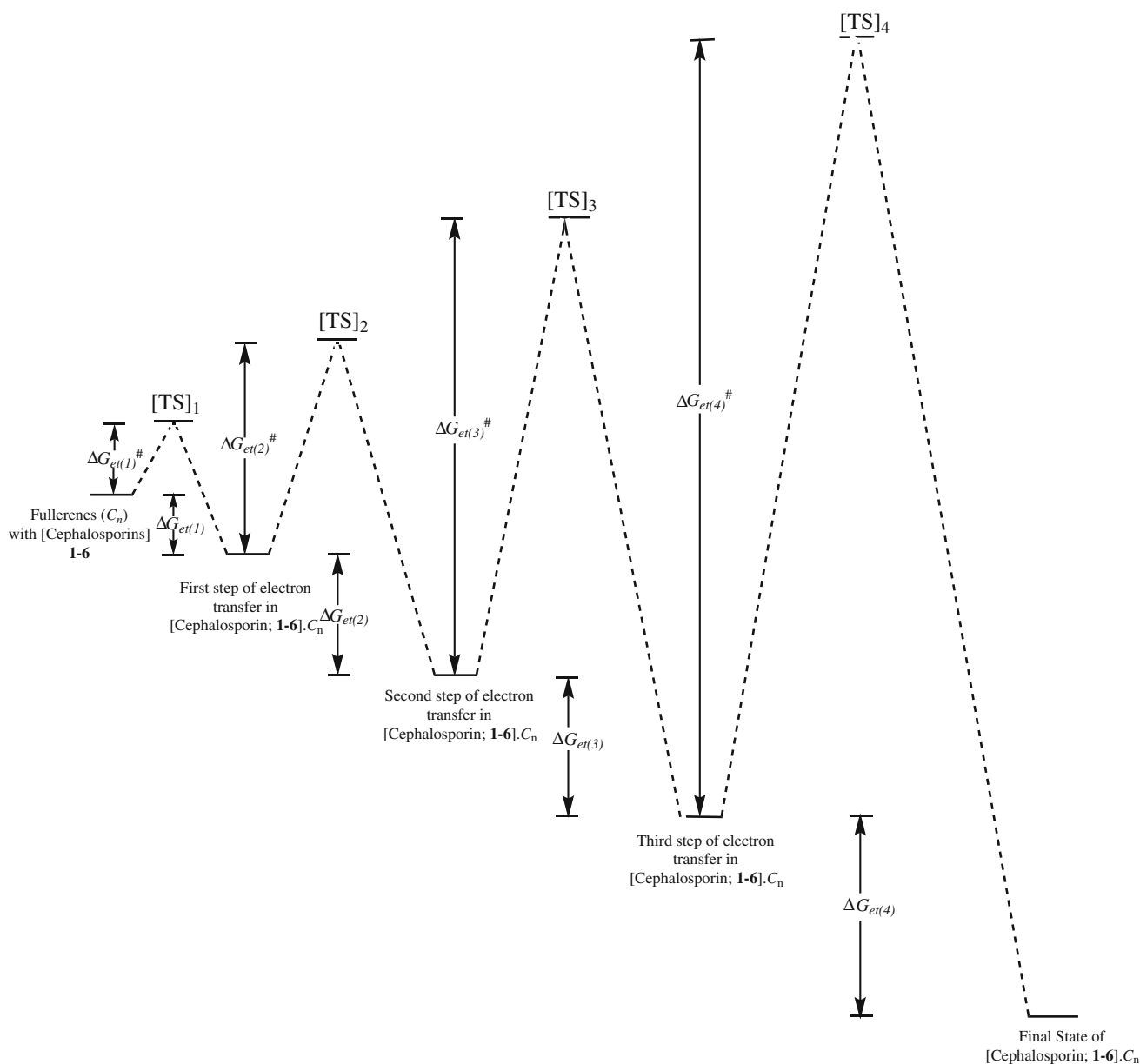
Fig. 3 The surfaces of the free energies of ET-process [$\Delta G_{\text{et}(n)}$ and $\Delta G_{\text{et}(n)}^{\#}$ ($n = 1$–4)] between **1** and **6** and fullerenes in **7–60** complexes

for structures **7–60**. The free energies were calculated with Eqs. 1–23 and are shown in Tables 1, 2, 3, 4, 5 6, 7, 8, 9 and 10.

We determined the values of the maximum wavelengths ($\lambda_{(n)}$; $n = 1$–4; in nm) for each stage of the electron transfer process in the nanostructure supramolecular complexes with *Planck's* formula. Using this formula, was also determined the photonic energy of the electron transfer process. Most of the values were found in the UV (200–360 nm) range of the electromagnetic spectrum. The maximum wavelengths ($\lambda_{(n)}$; $n = 1$–4) depended on the $\Delta G_{\text{et}(n)}^{\#}$ value in each stage. The values of the maximum

wavelengths ($\lambda_{(n)}$; $n = 1$–4) were increased by decreasing the $\Delta G_{\text{et}(n)}^{\#}$ value in each stage.

In this study, was investigated the photo-electron transfer process to find more medicinal activity properties for the cephalosporin antibiotics **1–6** in the presence of the selected fullerenes by performing the supramolecular complexes [cephalosporin antibiotics **1–6**]·C_n. The cephalosporin–fullerene supramolecular complexes and the calculated values of $\Delta G_{\text{et}(n)}$, $\Delta G_{\text{et}(n)}^{\#}$ and $\lambda_{(n)}$ ($n = 1$–4) corresponding to these complexes have not been reported before.

Conclusion

In this study, were shown the relationship between the number of carbon atoms and the four free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$) of fullerenes C_n ($n = 60$, 70, 76, 82 and 86) with cefadroxil, cefepime, cephalexin, cefotaxime, cefoperazone and ceftriaxone on the basis of the four reduction potentials ($^{Red.}E_1$–$^{Red.}E_4$) of the fullerenes. The antibiotics **1–6** and fullerenes have important electron-transfer properties as the most well-known cephalosporin antibiotics (β-lactam class of antibiotics) and molecular conductors. The electrochemical data of the cephalosporin-fullerene complexes are reported here. These results include the four free energies of electron transfer ($\Delta G_{et(1)}$–$\Delta G_{et(4)}$), calculated using the Rehm-Weller equation, $\Delta G_{et(n)}^{\#}$ and $\lambda_{(n)}$ ($n = 1$–4), using the Marcus theory. Using the number of carbon atoms in the fullerene molecules and the model equations, the structural relationships between the aforementioned physicochemical data can be derived. These equations allow one to calculate $\Delta G_{et(n)}$ ($n = 1$–4), $\Delta G_{et(n)}^{\#}$ and $\lambda_{(n)}$ ($n = 1$–4) for cephalosporin antibiotics **1–6**, as [cefadroxil]·C_n **7–11** and **37–40**; [cefepime]·C_n, **12–16** and **41–44**; [cephalexin]·C_n, **17–21** and **45–48**; [cefotaxime]·C_n, **22–26** and **49–52**; [cefoperazone]·C_n, **27–31** and **53–56** and [ceftriaxone]·C_n, **32–36** and **57–60** (supramolecular complexes **7–60**) of the fullerenes (C_{60}, C_{70}, C_{76}, C_{82}, C_{86}, C_{78}, C_{84} and C_{120}). One of the other aspects of this study was the investigation of the photo-electron transfer process to find more medicinal activity conditions and properties for the antibiotics **1–6** in the presence of the selected fullerenes by performing the supramolecular complexes [antibiotics **1–6**]·C_n. The novel supramolecular complexes discussed have neither been synthesized nor reported before.

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