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Theoretical Study of Structural Relationships and Electrochemical Properties of [DNA-Nucleotide Bases]@C_n Complexes

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ABSTRACT

The primary structure of both DNA and RNA consists of a polymeric chain of nucleotides. Nucleotides are the basic monomer building block units in the nucleic acids. A nucleotide is composed of a nucleobase (nitrogenous base) and a five-carbon sugar (either ribose or 2'-deoxyribose), and one to three phosphate groups. Together, the nucleobase and sugar comprise a nucleoside. The DNA nucleotide bases are guanine (G) and adenine (A), and the pyrimidine bases are thymine (T) and cytosine (C). The voltammetric oxidation of all deoxyribonucleic acid (DNA) monophosphate nucleotides was investigated before. Since the discovery of fullerenes (C_n), one of the main classes of carbon compounds, the unusual structures and physicochemical properties of these molecules have been discovered, and many potential applications and physicochemical properties have been introduced. Up to now, various empty carbon fullerenes with different numbers "n," such as C₆₀, C₇₀, C₇₆, C₈₂ and C₈₆, have been obtained. Topological indices are digital values that are assigned based on chemical composition. These values are purported to correlate chemical structures with various chemical and physical properties. They 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 the fullerenes was used as an index to establish a relationship between the structures of guanine (G), adenine (A), thymine (T) and cytosine (C), 1-4 and fullerenes C_n (n=60, 70, 76, 82 and 86), which create [DNA-Nucleotide bases]@C_n, A-1 to A-5 ([Guanine]@C_n), B-1 to B-5 ([Adenine]@C_n), C-1 to C-5 ([Thymine]@C_n) and D-1 to D-5 ([Cytosine]@C_n). The relationship between the number of carbon atoms and the free energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) are assessed using the Rehm-Weller equation for A-1 to A-5, B1 to B-5, C-1 to C-5 and D-1 to D-5 supramolecular [DNA-Nucleotide bases]@C_n complexes 5-24. Calculations are presented for the four reduction potentials ($^{Red}E_1$ to $^{Red}E_4$) of fullerenes C_n. The results were used to calculate the four free-energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of supramolecular complexes A-1 to A-18 to B-1 to B-18, C-1 to C-18 and D-1 to D-18 (5-76) for fullerenes C₆₀ to C₃₀₀.

Key words: Fullerenes; DNA; Nucleotide bases; Rehm-Weller equation;
Free energy of electron transfer; Electrochemical properties; Reduction potential.

INTRODUCTION

Many studies of the chemical, physical and mechanical properties of empty and endohedral fullerenes have been carried out¹⁻¹⁵. 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 by Shen^{2,15}. The unique stability of molecular allotropes such as C_{60} and C_{70} , was demonstrated in 1985^{1,2}. This event led to the discovery of a whole new set of carbon-based substances, known as fullerenes.

After the discovery of C_{60} peapods by Luzzi *et al.*³⁻⁸, the aligned structure of encapsulated molecules, due to the molecule-molecule and/or molecule-SWNT interactions, has been studied as a new type of hybrid material^{5,6}. Zhang *et al.*³ reported evidence for the latter interaction measuring the thermal stability of C_{60} peapods³⁻⁷.

The electrochemical properties of the C_{60} fullerene have been studied since the early 1990s, when these materials first became available in macroscopic quantities (for a review, see⁵)^{4,5}. In 1990, Haufler *et al.*⁶ showed that CH_2Cl_2 electrochemically reduces C_{60} to C_{60}^{1-} and C_{60}^{2-} . In 1992, Echegoyen *et al.*⁷ cathodically reduced C_{60} in six reversible one-electron steps for $-0.97V$ vs. Fc/Fc^+ (Fc =ferrocene). This fact, along with the inability to perform anodic electrochemistry on fullerenes, matches the electronic structure of fullerenes: the LUMO of C_{60} can accept up to six electrons to form C_{60}^{6-} , but the position of the HOMO does not allow for hole-doping under the usual reported electrochemical conditions. In 1991, Bard *et al.*⁸ first reported on the irreversible electrochemical and structural reorganization of solid fullerenes in acetonitrile. Dunsch *et al.*⁹ improved upon the experimental conditions by investigating highly organized C_{60} films on HOPG, in an aqueous medium. The reduction of these films induces a morphological change; they re-structure

Table 1: The data values on the Guanine (G) A-1 to A-5 and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol⁻¹, between Guanine with C_n (as [G]@ C_n compounds A-6 to A-18) (forms 5-9 and 25-37) supramolecular complexes

No.	Row	*Formula of [TC]@ C_n	(ΔG_{et}) in kcal mol ⁻¹ [G]@ C_n			
			$\Delta G_{et(1)}$ *	$\Delta G_{et(2)}$ *	$\Delta G_{et(3)}$ *	$\Delta G_{et(4)}$ *
5	A-1	[G]@ C_{60}	43.13 (41.28)	50.35 (50.04)	62.50 (60.42)	74.35 (71.02)
6	A-2	[G]@ C_{70}	42.42 (40.59)	48.94 (49.58)	59.99 (58.57)	71.53 (68.49)
7	A-3	[G]@ C_{76}	39.79 (37.13)	45.41 (44.51)	58.29 (55.11)	69.55 (64.568)
8	A-4	[G]@ C_{82}	35.50 (31.36)	39.86 (39.43)	56.45 (51.89)	67.35 (60.19)
9	A-5	[G]@ C_{86}	31.72 (28.82)	35.04 (35.05)	55.14 (52.35)	65.77 (60.65)
25	A-6	[G]@ C_{78}	38.54	43.78	57.694	68.842
26	A-7	[G]@ C_{84}	33.698	37.558	55.804	66.574
27	A-8	[G]@ C_{120}	-30.13	-42.11	41.44	48.43
28	A-9	[G]@ C_{132}	-64.654	-84.794	35.5	40.654
29	A-10	[G]@ C_{140}	-91.35	-117.73	31.22	34.99
30	A-11	[G]@ C_{146}	-113.304	-144.784	27.842	30.49
31	A-12	[G]@ C_{150}	-128.86	-163.94	25.51	27.37
32	A-13	[G]@ C_{160}	-170.97	-215.75	19.4	19.15
33	A-14	[G]@ C_{162}	-179.944	-226.784	18.13	17.434
34	A-15	[G]@ C_{240}	-673.45	-831.83	-43.88	-68.21
35	A-16	[G]@ C_{276}	-995.614	-1225.994	-80.708	-120.05
36	A-17	[G]@ C_{288}	-1116.25	-1373.51	-94.136	-139.058
37	A-18	[G]@ C_{300}	-1243.51	-1529.09	-108.14	-158.93

The data of $\Delta G_{et(n)}$ ($n=1-4$) were predicted by using Eq. 2 to Eq. 5, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1).

into conductive nanoclusters of ~100 nm in diameter^{9,10-15}.

DNA nanotechnology uses the unique molecular recognition properties of DNA and other nucleic acids to create self-assembling branched DNA complexes with useful properties. DNA is thus used as a structural material rather than as a carrier of biological information. This has led to the creation of two-dimensional periodic lattices (both tile-based as well as using the "DNA origami" method) as well as three-dimensional structures in the shapes of polyhedra. Nanomechanical devices and algorithmic self-assembly have also been demonstrated, and these DNA structures have been used to template the arrangement of other molecules such as gold nanoparticles and streptavidin proteins¹⁶.

Chemical modification of each of the DNA bases causes molecular disturbance to the genetic

machinery that leads to cell malfunction and death. The purine bases, guanine (G) and adenine (A), and the pyrimidine bases, thymine (T) and cytosine (C), are fundamental compounds in biological systems, participating in processes as distinct as energy transduction, metabolic cofactors and cell signaling, and are essential building blocks of nucleic acids^{17,18}. The study of DNA oxidative damage is of great importance since it is well established that it constitutes an important source of genomic instability.

Voltammetric methods are suitable to study DNA oxidation, but almost all previous studies focus only on the oxidation of purine derivative compounds. The voltammetric results presented in this work extend previous voltammetric studies on DNA to include all four bases (G, A, T and C, 1-4) and corresponding nucleotides¹⁷. It is well established that the oxidation of DNA is an important

Table 2: The data values on the Adenine (A) B-1 to B-5 and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol⁻¹, between Adenine with C_n (as [A]@C_n compounds B-6 to B-18) (forms 10-14 and 38-50) supramolecular complexes. The data of $\Delta G_{et(n)}$ (n=1-4) were predicted by using Eq. 6 to Eq. 9, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

No.	Row	*Formula of [A]@C _n	(ΔG_{et}) in kcal mol ⁻¹ [A]@C _n			
			$\Delta G_{et(1)}$ *	$\Delta G_{et(2)}$ *	$\Delta G_{et(3)}$ *	$\Delta G_{et(4)}$ *
10	B-1	[A]@C ₆₀	49.12 (47.27)	56.35 (60.65)	68.49 (71.02)	80.34 (81.63)
11	B-2	[A]@C ₇₀	48.41(46.58)	54.94 (60.19)	65.98 (69.18)	77.52 (79.10)
12	B-3	[A]@C ₇₆	45.78 (43.12)	51.41(55.11)	64.28 (65.72)	75.54 (75.18)
13	B-4	[A]@C ₈₂	41.49 (37.36)	45.86 (50.04)	62.44 (62.50)	73.34 (70.79)
14	B-5	[A]@C ₈₆	37.71 (34.82)	41.04 (45.66)	61.13 (62.94)	71.76 (71.25)
38	B-6	[A]@C ₇₈	44.53	49.78	63.684	74.832
39	B-7	[A]@C ₈₄	39.688	43.558	61.794	72.564
40	B-8	[A]@C ₁₂₀	-24.14	-36.11	47.43	54.42
41	B-9	[A]@C ₁₃₂	-58.664	-78.794	41.49	46.644
42	B-10	[A]@C ₁₄₀	-85.36	-111.73	37.21	40.98
43	B-11	[A]@C ₁₄₆	-107.314	-138.784	33.832	36.48
44	B-12	[A]@C ₁₅₀	-122.87	-157.94	31.5	33.36
45	B-13	[A]@C ₁₆₀	-164.98	-209.75	25.39	25.14
46	B-14	[A]@C ₁₆₂	-173.954	-220.784	24.12	23.424
47	B-15	[A]@C ₂₄₀	-667.46	-825.83	-37.89	-62.22
48	B-16	[A]@C ₂₇₆	-989.624	-1219.994	-74.718	-114.06
49	B-17	[A]@C ₂₈₈	-1110.26	-1367.51	-88.146	-133.068
50	B-18	[A]@C ₃₀₀	-1237.52	-1523.09	-102.15	-152.94

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

source of genomic instability since there is evidence that the oxidation products of DNA bases play important roles in mutagenesis, carcinogenesis, aging, and age-related disease^{17,19-22}. Electrochemical methods are very promising for the study of DNA oxidative damage and in the investigation of the mechanisms of interaction of drugs with DNA.^{17,23-25}

Graph theory has been a useful tool in assessing the QSAR (Quantitative Structure Activity Relationship) and QSPR (Quantitative Structure Property Relationship)²⁶⁻⁴⁰. Numerous studies in different areas have used topological indices (TI). [27-36. It is important to use effective mathematical methods to make good correlations between several properties of chemicals. In 1993 and 1997, several complex applications of the indices were reported²⁷⁻⁴⁰. The numbers of carbon atoms in the structures of the fullerenes were used as the index here.

This study shows the relationship between the number of carbon atoms and the four free energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of fullerenes C_n ($n=60, 70, 76, 82$ and 86), on the basis of the four reduction potentials ($^{Red}E_i$ to $^{Red}E_4$), as assessed by applying the Rehm-Weller equation[41] to create [DNA-Nucleotide bases]@ C_n , A-1 to A-5 ([Guanine]@ C_n), B-1 to B-5 ([Adenine]@ C_n), C-1 to C-5 ([Thymine]@ C_n) and D-1 to D-5 ([Cytosine]@ C_n) 20-24. The results were extended to calculate the four free energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of other supramolecular complexes of guanine (G), adenine (A), thymine (T) and cytosine (C) 1-4,, with fullerenes C_{60} to C_{300} ([Tetracyclines]@ C_n , complexes 5-76). This study calculated the four free energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of A-1 to A-18, B-1 to B-18, C-1 to C-18 and D-1 to D-18. See Equations 1 to 17, Tables 1-4 and Figs. 1-2.

Table 3: The data values on the Thymine (T) C-1 to C-5 and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol⁻¹, between Thymine with C_n (as [T]@ C_n compounds C-6 to C-18) (forms 15-19 and 51-63) supramolecular complexes. The data of $\Delta G_{et(n)}$ ($n=1-4$) were predicted by using Eq. 6 to Eq. 9, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

No.	Row	*Formula of [T]@ C_n	(ΔG_{et}) in kcal mol ⁻¹ [T]@ C_n			
			$\Delta G_{et(1)}$ *	$\Delta G_{et(2)}$ *	$\Delta G_{et(3)}$ *	$\Delta G_{et(4)}$ *
15	C-1	[T]@ C_{60}	53.74 (51.89)	60.96 (60.65)	73.10 (71.02)	84.9 (81.63)
16	C-2	[T]@ C_{70}	53.03 (51.19)	59.55 (60.19)	70.59 (69.18)	82.14 (79.10)
17	C-3	[T]@ C_{76}	50.40 (47.73)	56.02 (55.11)	68.89 (65.72)	80.16 (75.18)
18	C-4	[T]@ C_{82}	46.11 (41.97)	50.47 (50.04)	67.05 (62.50)	77.96 (70.79)
19	C-5	[T]@ C_{86}	42.33 (39.43)	45.65 (45.66)	65.74 (62.95)	76.38 (71.25)
51	C-6	[T]@ C_{78}	49.15	54.39	68.294	79.452
52	C-7	[T]@ C_{84}	44.308	48.168	66.404	77.184
53	C-8	[T]@ C_{120}	-19.52	-31.5	52.04	59.04
54	C-9	[T]@ C_{132}	-54.044	-74.184	46.1	51.264
55	C-10	[T]@ C_{140}	-80.74	-107.12	41.82	45.6
56	C-11	[T]@ C_{146}	-102.694	-134.174	38.442	41.1
57	C-12	[T]@ C_{150}	-118.25	-153.33	36.11	37.98
58	C-13	[T]@ C_{160}	-160.36	-205.14	30	29.76
59	C-14	[T]@ C_{162}	-169.334	-216.174	28.73	28.044
60	C-15	[T]@ C_{240}	-662.84	-821.22	-33.28	-57.6
61	C-16	[T]@ C_{276}	-985.004	-1215.384	-70.108	-109.44
62	C-17	[T]@ C_{288}	-1105.64	-1362.9	-83.536	-128.448
63	C-18	[T]@ C_{300}	-1232.9	-1518.48	-97.54	-148.32

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

Graphing and Mathematical Method

All graphs were generated using the *Microsoft Office Excel 2003* program. Using the number of carbon atoms contained within the C_n fullerenes, several valuable properties of the fullerenes can be calculated. The values were used to calculate the four free energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$), according to the Rehm-Weller equation for [DNA-Nucleotide bases]@ C_n , A-1 to A-5 ([Guanine]@ C_n), B-1 to B-5 ([Adenine]@ C_n), C-1 to C-5 ([Thymine]@ C_n) and D-1 to D-5 ([Cytosine]@ C_n) compounds 5-24.

Both linear (MLR:Multiple Linear Regressions) and nonlinear (ANN:Artificial Neural Network) models were used in this study. Equations 1-17 were utilized to calculate the remaining values of $\Delta G_{et(1)}$ to $\Delta G_{et(4)}$ for complexes that have yet to be reported in the literature. Some of the other indices

were examined, and the best results and equations for extending the physicochemical data were chosen^{31,32,37-40}.

The Rehm-Weller equation estimates the free energy change between an electron donor (D) and an acceptor (A) as [47]

$$\Delta G^\circ = e[E_D^{\circ} - E_A^\circ] - \Delta E + w_1, \quad \dots(1)$$

where e is the unit electrical charge, E_D° and E_A° are the reduction potentials of the electron donor and acceptor, respectively, ΔE is the energy of the singlet or triplet excited state, and w_1 is the work required to bring the donor and acceptor to within the electron transfer (ET) distance. If an electrostatic complex forms before the electron transfer, the work term in this expression is zero⁴¹.

Table 4: The data values on the Cytosine (C) D-1 to D-5 and the values of the 4 free energies of electron transfer (ΔG_{et}), in kcal mol⁻¹, between Cytosine with C_n (as [C]@ C_n compounds D-6 to D-18) (forms 20-24 and 64-76) supramolecular complexes. The data of $\Delta G_{et(n)}$ ($n=1-4$) were predicted by using Eq. 6 to Eq. 9, and those in parentheses were calculated by the Rehm-Weller equation (Eq. 1)

No.	Row	*Formula of [C]@ C_n	(ΔG_{et}) in kcal mol ⁻¹ [C]@ C_n			
			$\Delta G_{et(1)}$ *	$\Delta G_{et(2)}$ *	$\Delta G_{et(3)}$ *	$\Delta G_{et(4)}$ *
20	D-1	[C]@ C_{60}	57.20 (55.34)	64.42 (64.11)	76.56 (74.48)	88.41(85.09)
21	D-2	[C]@ C_{70}	56.49 (54.65)	63.01(63.65)	74.05 (72.64)	85.59 (82.55)
22	D-3	[C]@ C_{76}	53.86 (51.19)	59.48 (58.57)	72.35 (69.18)	83.61 (78.64)
23	D-4	[C]@ C_{82}	49.57 (45.43)	53.93 (53.50)	70.51 (65.95)	81.41 (74.25)
24	D-5	[C]@ C_{86}	45.79 (45.43)	49.11 (49.12)	69.20 (66.41)	79.83 (74.71)
64	D-6	[C]@ C_{78}	52.61	57.85	71.754	82.902
65	D-7	[C]@ C_{84}	47.768	51.628	69.864	80.634
66	D-8	[C]@ C_{120}	-16.06	-28.04	55.5	62.49
67	D-9	[C]@ C_{132}	-50.584	-70.724	49.56	54.714
68	D-10	[C]@ C_{140}	-77.28	-103.66	45.28	49.05
69	D-11	[C]@ C_{146}	-99.234	-130.714	41.902	44.55
70	D-12	[C]@ C_{150}	-114.79	-149.87	39.57	41.43
71	D-13	[C]@ C_{160}	-156.9	-201.68	33.46	33.21
72	D-14	[C]@ C_{162}	-165.874	-212.714	32.19	31.494
73	D-15	[C]@ C_{240}	-659.38	-817.76	-29.82	-54.15
74	D-16	[C]@ C_{276}	-981.544	-1211.924	-66.648	-105.99
75	D-17	[C]@ C_{288}	-1102.18	-1359.44	-80.076	-124.998
76	D-18	[C]@ C_{300}	-1229.44	-1515.02	-94.08	-144.87

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

DISCUSSION

Most electrochemical DNA biosensors are based on the determination of purine oxidation peaks, principally the guanine peak, to monitor the degree of oxidative damage caused to DNA^{17,23-25,42}. This is due to the fact that guanine has the lowest oxidation potential of all DNA bases^{17,22,43}. Several studies showed the importance of considering the influence on the chemical reactivity of DNA

nucleotide bases 1-4 of the chemical environment surrounding the bases residues in DNA (which is determined by base sequence). For instance, it has been shown that cytosine hydrogen bond interaction with guanine affects the rate of guanine oxidation within the double helix of DNA^{17,44}. Mechanistic studies on the electrochemical behavior of purine and pyrimidine derivatives have been performed. Oxidation of purine derivative compounds was extensively studied at solid electrodes, mainly

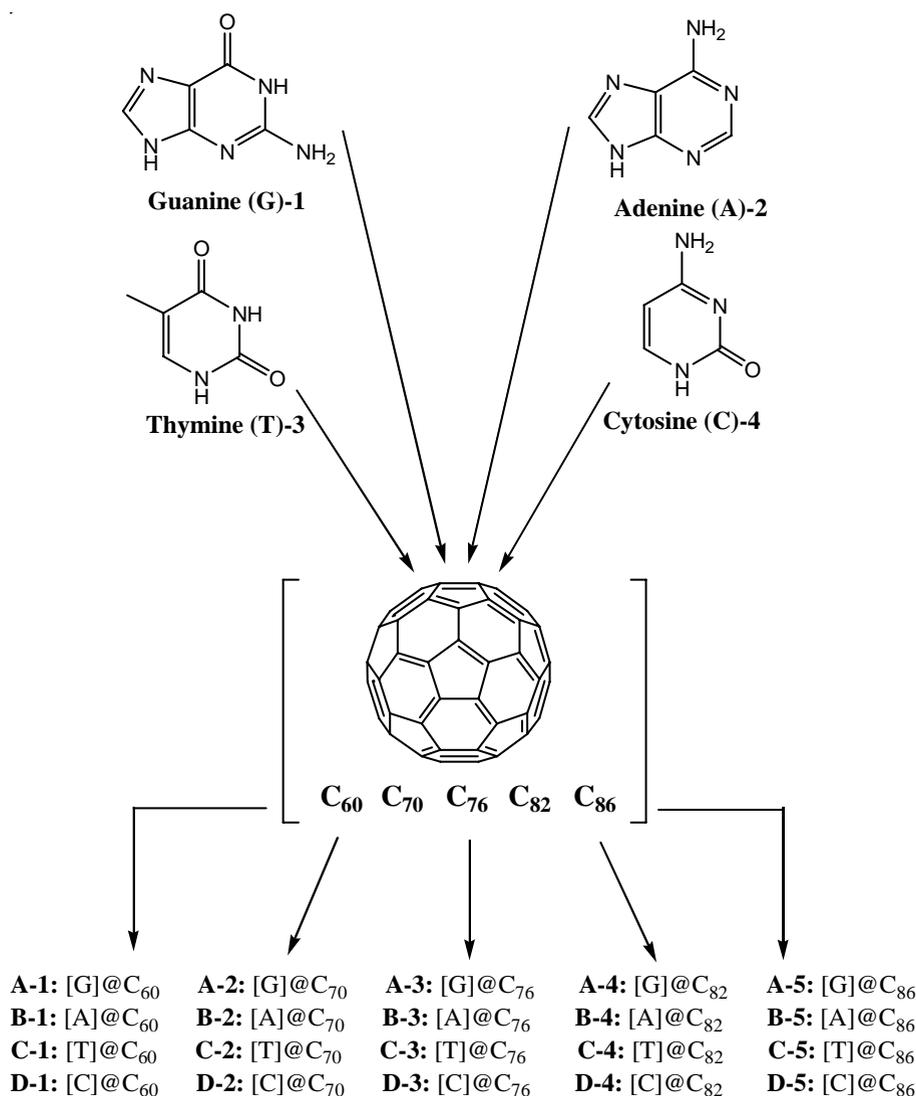


Fig. 1: The conjectured structures of Guanine (G), Adenine (A), Thymine (T) and Cytosine (C) 1-4 and fullerenes C_n (n=60, 70, 76, 82 and 86) which create [DNA-Nucleotide bases]@C_n, A-1 to A-5 ([G]@C_n), B-1 to B-5 ([A]@C_n), C-1 to C-5 ([T]@C_n) and D-1 to D-5 ([C]@C_n)

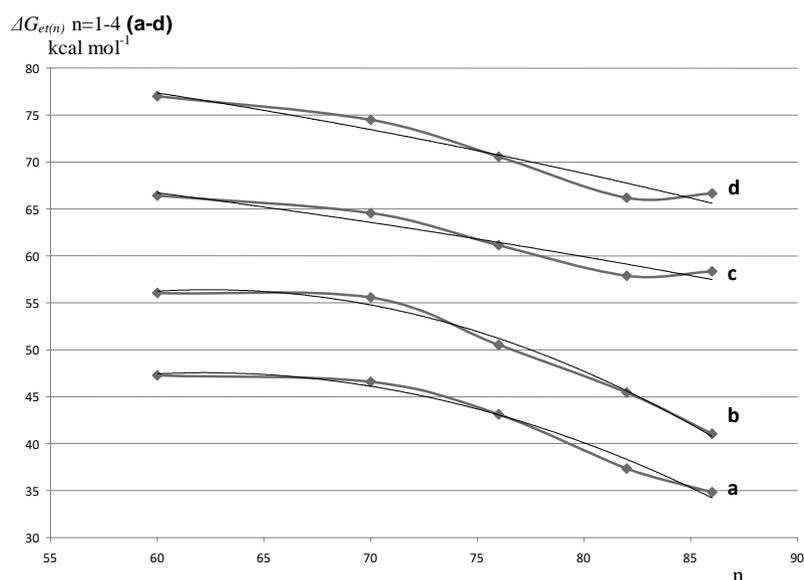
carbonbased Electrodes^{17,21,22}. The electroactivity of pyrimidine derivative compounds at solid electrodes has been shown.^{17,45-47}. This led to the possibility of detecting voltammetrically the oxidation of all DNA bases at glassy carbon electrodes (GCEs) and confirmed that guanine and adenine are more easily detected than thymine and cytosine. This was done using sonovoltammetry, but the simultaneous sonovoltammetric detection of the four DNA bases was achieved only in alkaline electrolyte solutions containing pyrimidine bases with a concentration 10 times higher than the purine base concentration^{17,47-49}.

The differential pulse voltammogram obtained for a mixture of 200 μ M guanine and adenine and 200IM thymine and cytosine in pH 7.4, 0.1M phosphate buffer supporting electrolyte solution using a 3-mm-diameter GCE shows four oxidation peaks of the same height magnitude. It was reported that the peak at 0.70V is attributed to G oxidation, the easiest oxidizable of all DNA bases^{21,22,43,47}. The oxidation potentials are 0.96V^{17,47,49-51}, 1.16 V, and 1.31V.[17-21] for A, T and C, respectively.

Here, we calculated four free energies of electron transfer ($DG_{et(1)}$ to $DG_{et(4)}$) of other supramolecular complexes of of guanine (G), adenine (A), thymine (T) and cytosine (C),, with fullerenes C_{60} to C_{300} ([DNA-Nucleotide bases] $@C_n$, complexes 5-76).

The four reported reduction potentials ($^{Red}E_1$ to $^{Red}E_4$) of fullerenes C_n are as follows: for C_{60} are, -1.12, -1.50, -1.95 and -2.41V, respectively. [52] The $^{Red}E_n$ (Volt, n=1-4) for C_{70} are -1.09, -1.48, -1.87 and -2.30V, respectively. [52] The values of $^{Red}E_n$ (Volt, n=1-4) for C_{76} are -0.94, -1.26, -1.72 and -2.13V, respectively. [52] Four values of $^{Red}E_n$ (Volt, n=1-4) for C_{82} are -0.69, -1.04, -1.58 and -1.94V, respectively. [52] The $^{Red}E_n$ (Volt, n=1-4) for C_{86} are -0.58, -0.85, -1.60 and -1.96V, respectively.[52] C_{180} and C_{240} have not been prepared or isolated among the fullerenes which they have listed in Tables 1-4.

Tables 1-4 contain a summary of the data. They show the calculated values (5-76) of the four electron transfer free energies ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) in kcal mol⁻¹) between nucleotide bases 1-4 as [DNA-Nucleotide bases] $@C_n$ complexes and fullerenes



* The related curves for other forms have similar structures to Fig. 2 (a-d).

Fig. 2: The relationship between the number “n” of carbon atoms in the fullerenes and the first(a), second(b), third(c) and fourth(d) free-energies of electron transfer ($\Delta G_{et(n)}$) of [G] $@C_n$ (n = 60, 70, 76, 82 and 86), compounds A-1 to A-5

C_n ($n = 60, 70, 76, 82$ and 86). These values were calculated using the Rehm-Weller equation (Eq.-1). The selected tetracyclines (1-4) were used to model the structural relationship between the number of carbon atoms in the fullerenes and $\Delta G_{et(n)}$ ($n=1-4$). The data of compounds A-1 to A-18, B-1 to B-18, C-1 to C-18 and D-1 to D-18 are reported in the appropriate tables. Figure-1 depicts the structures of guanine (G), adenine (A), thymine (T) and cytosine (C) 1-4 and fullerenes C_n ($n=60, 70, 76, 82$ and 86) which create [DNA-Nucleotide bases]@ C_n , A-1 to A-5 ([Guanine]@ C_n), B-1 to B-5 ([Adenine]@ C_n), C-1 to C-5 ([Thymine]@ C_n) and D-1 to D-5 ([Cytosine]@ C_n).

Fig.-2 (graphs a-d) demonstrate the relationships between the number of carbon atoms of fullerenes "n" and the first, second, third and fourth free-energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of [Guanine]@ C_n ($n = 60, 70, 76, 82$ and 86). Equations 2-5 correspond to Fig. 2 (graphs a-d). This data was regressed with a second-order polynomial. The R-squared values (R^2) for these graphs are 0.9875, 0.9924, 0.9385 and 0.9477, respectively.

$$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9197(n) - 49.216 \quad \dots(2)$$

$$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4999(n) - 58.794 \quad \dots(3)$$

$$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0090(n) + 69.160 \quad \dots(4)$$

$$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1080(n) + 78.673 \quad \dots(5)$$

By using Equations 1-5, it is possible to calculate the values of $\Delta G_{et(1)}$ to $\Delta G_{et(4)}$ of [Guanine]@ C_n . Table 1 contains the calculated values of the free-energies of electron transfer ($\Delta G_{et(n)}$, $n=1-4$, in kcal mol⁻¹) between Guanine(G) 1 and C_n (as [G]@ C_n compounds A-1 to A-5) 5-9 supramolecular complexes. The $\Delta G_{et(n)}$ ($n=1-4$) for [G]@ C_n (C_{60} , C_{70} , C_{76} , C_{82} , C_{86} , C_{78} , C_{84} , C_{120} , C_{132} , C_{140} , C_{146} , C_{150} , C_{160} , C_{162} , C_{240} , C_{276} , C_{288} and C_{300}) are predicted by using Eq. 2-5 and the Rehm-Weller equation (see Table-1).

Equations 6-9 demonstrate the relationships between the number "n" of carbon atoms in the fullerenes and the first, second, third and fourth free-energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of [Adenine]@ C_n ($n = 60, 70, 76, 82$ and

86). These data were regressed with a second-order polynomial. The R-squared values (R^2) for these graphs are 0.9875, 0.9924, 0.9385 and 0.9477, respectively.

$$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9197(n) - 43.220 \quad \dots(6)$$

$$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4999(n) - 52.798 \quad \dots(7)$$

$$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0090(n) + 75.156 \quad \dots(8)$$

$$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1080(n) + 84.668 \quad \dots(9)$$

By using Equations 1 and 6-9, it is possible to calculate the values of $\Delta G_{et(1)}$ to $\Delta G_{et(4)}$ of [Adenine]@ C_n . Table-2 contains the seventy-two calculated values of the free energies of electron transfer ($\Delta G_{et(n)}$, $n=1-4$, in kcal mol⁻¹) between Adenine(A) 2 and the C_n (as [A]@ C_n compounds B-1 to B-5) 10-14 supramolecular complexes. The $\Delta G_{et(n)}$ ($n=1-4$) for [CTC]@ C_n (C_{60} , C_{70} , C_{76} , C_{82} , C_{86} , C_{78} , C_{84} , C_{120} , C_{132} , C_{140} , C_{146} , C_{150} , C_{160} , C_{162} , C_{240} , C_{276} , C_{288} and C_{300}) are predicted by using Eq. 6-9 and the Rehm-Weller equation (see Table-2).

The oxidation potentials (^{ox}E) of Thymine (T) 3 and Cytosine (C) 4 are equal to 1.16 and 1.31V, respectively. The Rehm-Weller equation shows the free-energies of electron transfer ($\Delta G_{et(n)}$, $n=1-4$, in kcal mol⁻¹) between the selected DNA nucleotide bases 3 & 4 and C_n . Equations 10 to 13 and equations 14 to 17 show the relationships between the number of carbon atoms of fullerenes "n" and the first, second, third and fourth free-energy of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$) of [Thymine]@ C_n and [Cytosine]@ C_n ($n = 60, 70, 76, 82$ and 86), respectively. These data were regressed with a second-order polynomial. The R-squared values (R^2) for the graphs of [Thymine]@ C_n are: 0.9875, 0.9924, 0.9385 and 0.9477, respectively.

$$DG_{et(1)} = -0.0235(n)^2 + 2.9197(n) - 38.608 \quad \dots(10)$$

$$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4999(n) - 48.186 \quad \dots(11)$$

$$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0090(n) + 79.768 \quad \dots(12)$$

$$\Delta G_{et(4)} = -0.0038(n)^2 + 0.1080(n) + 89.280 \quad \dots(13)$$

The R-squared values (R^2) for the graphs

related to equations 14 to 17 of [Cytosine]@C_n are: 0.9875, 0.9924, 0.9385 and 0.9477, respectively.

$$\Delta G_{et(1)} = -0.0235(n)^2 + 2.9197(n) - 35.149 \dots(14)$$

$$\Delta G_{et(2)} = -0.0280(n)^2 + 3.4999(n) - 44.727 \dots(15)$$

$$\Delta G_{et(3)} = -0.0025(n)^2 + 0.0090(n) + 83.227 \dots(16)$$

$$\Delta G_{et(4)} = -0.0050(n)^2 + 0.1080(n) + 92.739 \dots(17)$$

By using Equations 10-13 and 14-17, it is possible to calculate the values of $\Delta G_{et(1)}$ to $\Delta G_{et(4)}$ of [Thymine]@C_n and [Cytosine]@C_n. Tables 3 and 4 contain the calculated values of the free-energies of electron transfer ($\Delta G_{et(n)}$, n=1-4, in kcal mol⁻¹) between the selected DNA nucleotide bases 3 & 4 and C_n (as [T]@C_n C-1 to C-5 and [C]@C_n D-1 to D-5) 15-19 and 20-24 supramolecular complexes. The $\Delta G_{et(n)}$ (n=1-4) for [T]@C_n and [C]@C_n (C₆₀, C₇₀, C₇₆, C₈₂, C₈₆, C₇₈, C₈₄, C₁₂₀, C₁₃₂, C₁₄₀, C₁₄₆, C₁₅₀, C₁₆₀, C₁₆₂, C₂₄₀, C₂₇₆, C₂₈₈ and C₃₀₀) are predicted by using equations 10-13, 14-17 and the Rehm-Weller equation (see Tables 3 and 4).

By utilizing these results (Eq. 2-17) and the Rehm-Weller equation, the electron transfer energies of $\Delta G_{et(n)}$ (n=1-4) of the complexes between DNA nucleotide bases (G, A, T and C) 1-4 with fullerenes (C₆₀, C₇₀, C₇₆, C₈₂, C₈₆, C₇₈, C₈₄, C₁₂₀, C₁₃₂, C₁₄₀, C₁₄₆, C₁₅₀, C₁₆₀, C₁₆₂, C₂₄₀, C₂₇₆, C₂₈₈ and C₃₀₀) were approximated (Tables 1 to 4). The calculated values of the free electron transfer energies of $\Delta G_{et(n)}$ (n=1-4) for selected [DNA-Nucleotide bases]@C_n (n = 60, 70, 76, 82 and 86, compounds 5 to 76) in the Rehm-Weller equation and Eq. 2-17, are compared in Tables 1-4. There was good agreement between the calculated and the predicted values. In lieu of increasing the number of carbons atoms in the fullerene structure, the values of $\Delta G_{et(n)}$ (n=1-4) were decreased. It seems that electron transfer increases as the electron population in the C_n

structures increases. Tables 1-4 indicate that these results are related to the HOMO and LUMO gap of the fullerenes. The Tables also shows that some of the free electron transfer energies $\Delta G_{et(n)}$ (n=1-4) values of [G]@C_n, [A]@C_n, [T]@C_n and [C]@C_n are negative. The supramolecular complex structures which were discussed here, and the calculated values of $\Delta G_{et(n)}$ (n=1-4) corresponding to these supramolecular complexes were neither synthesized nor reported before.

CONCLUSION

Tetracyclines 1-4 and fullerenes have important pharmaceutical and physicochemical properties. The electrochemical data of the DNA nucleotide bases (G, A, T and C) 1-4, i.e. [G]@C_n, [A]@C_n, [T]@C_n and [C]@C_n were reported here. These include the four free-energies of electron transfer ($\Delta G_{et(1)}$ to $\Delta G_{et(4)}$), calculated using the Rehm-Weller equation for A-1 to A-5, B1 to B-5, C-1 to C-5 and D-1 to D-5 supramolecular complexes. Using the number of carbon atoms (n), along with the equations of the model, one can derive sound structural relationships between the aforementioned physicochemical data. By using the equations of this model, was calculated a good approximation for $\Delta G_{et(1)}$ to $\Delta G_{et(4)}$ for the DNA nucleotide bases 1-4 as [G]@C_n, [A]@C_n, [T]@C_n and [C]@C_n supramolecular complexes (A-1 to A-18, B-1 to B-18, C-1 to C-18 and D-1 to D-18) of the fullerenes (C₆₀, C₇₀, C₇₆, C₈₂, C₈₆, C₇₈, C₈₄, C₁₂₀, C₁₃₂, C₁₄₀, C₁₄₆, C₁₅₀, C₁₆₀, C₁₆₂, C₂₄₀, C₂₇₆, C₂₈₈ and C₃₀₀). The novel supramolecular complexes discussed have neither been synthesized nor reported previously.

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