Relationship study of octanol-water partitioning coefficients and total biodegradation of linear simple conjugated polyene and carotene compounds by use of the *Randić* index and maximum UV wavelength

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Topological indices are numerical values associated with chemical constitution that are purported to correlate chemical structure with various physical properties, chemical reactivity or biological activity. Graph theory is a delightful basis for the exploration of proof techniques in discrete mathematics, and its results have applications in many areas of science. One of the useful indices for examining structure-property relationships is the *Randić* index. In this study, we present the relationship between the *Randić* index, the logarithm of calculated octanol–water partitioning coefficients, and total biodegradation ($\log K_{ow}$ and TB_d ($mol\,h^{-1}$), respectively) with the maximum UV wavelength (λ_{max}) and ΔE ($\Delta E = hc/\lambda_{max}$), as the difference energy level of the HOMO and LUMO orbitals, for the linear simple conjugated polyenes. The results are extended for some of the carotene compounds. The interesting results of relating $\log K_{ow}$, TB_d, λ_{max}, ΔE, and the Randić index for these compounds are presented.

Keywords: octanol–water partitioning coefficient; biodegradation; *Randić* index; natural polyenes

1. Introduction

A survey of the different useful applications of graph theory obviously shows that this area is an exploration of techniques in discrete mathematics, and its results can be applied to various fields of sciences. Graph theory has been found to be an effective tool in 'QSAR' and 'QSPR' [1–6]. A graph is a topological concept rather than a geometrical concept of fixed geometry, and hence, Euclidean metric lengths, angles and three-dimensional spatial configurations have no meaning. Numerous studies have been made relating to the aforementioned fields using what are called topological indices (TI) [6]. All these applications have proven that one can utilise topological indices as very useful for molecular structure studies, as for the description and prediction of chemical and structural properties, biological and toxicological characters of compounds. One of the

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stages of TIs started when M. *Randić* introduced the molecular branching index [7]. In 1975, *Randić* proposed a TI that has become one of the most widely used in both QSAR and QSPR studies. However, the most important contribution at this stage is probably the great number of applications of TIs in several fields of chemistry. The TIs are based on the original idea of *Randić* of molecular branching, but were extended to account for contributions coming from path clusters, clusters and chains of different lengths [8–15]. The revival of research on TIs probably began in the 1990s, and by the middle of this decade the number of studies and applications of TIs in chemistry had increased [16,17]. Among the successful TIs in these applications are the molecular connectivity indices [16,18], including the *Randić* index [7], *Randić* index [9], the indices of Kier [20] electro topological state indices [21], the Balaban index [22] and the Wiener index [23]. N. Trinajstić and coworkers reported that 39 topological indices are presently available in the literature [24]. Estrada has made important studies in terms of generalised TIs with several topological indices in the graph invariant [25]. M. *Randić* introduced a useful and effective series of rules for the definition of TIs in chemical structure investigations, and the extension of applications to more complex situations in medicinal chemistry. A study of the structural relationship between some properties of simple conjugated polyenes and the *Randić* index was reported [26]. Effective and useful mathematical methods are needed for making good correlations between several chemical properties, medicinal chemistry and biological activity of chemicals. The octanol–water partition coefficient (K_{ow}) is a measure of the equilibrium concentration of a compound between octanol and water that indicates the potential for partitioning into soil organic matter (i.e. a high K_{ow} indicates a compound, that will preferentially partition into soil organic matter rather than water). This coefficient is inversely related to the solubility of a compound in water. The $\log K_{ow}$ is used in models to estimate plant and soil invertebrate bioaccumulation factors. Log K_{ow} is commonly used in QSAR studies and drug design, since this property is also related to drug absorption, bioavailability, metabolism and toxicity. This parameter is also used in many environmental studies to help determine the environmental fate of chemicals [27–29]. It has quite a lot of use in medicine and medicinal chemistry. Biodegradation (TB_d) is another useful and important factor in chemical and biochemical studies [28]. In this study, we will consider the relationship of the *Randić* index, the logarithm of calculated octanol–water partitioning coefficients, and total biodegradation, $\log K_{ow}$ and TB_d (mol h^{-1}), respectively, with the maximum UV wavelength (λ_{max}) and $\Delta E (\Delta E = hc/\lambda_{max})$ for the linear simple conjugated polyenes (**group-I**). The results will be considered for application to carotene compounds like α-carotene, β-carotene, γ-carotene, ε-carotene and lycopene (**group-II**).

$$H - \left[HC = CH \right]_{n_x} H$$
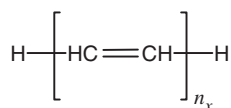
$$n_x = 1, 2, 3, \ldots, 11$$

Polyenes group (**I**)

These carotenes are some of the more than 500 members of the carotenoid family. These substances form the colouring pigments for deep yellow, orange and dark green fruits and vegetables. The compounds **I** represent initial members of polymerisation of acetylene and group-**II** are one of the great important groups of organic pigment and antioxidant agents that are found in natural sources.
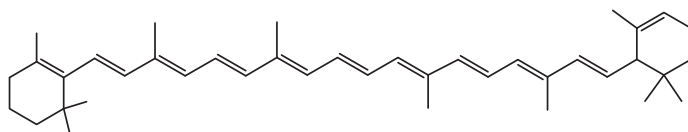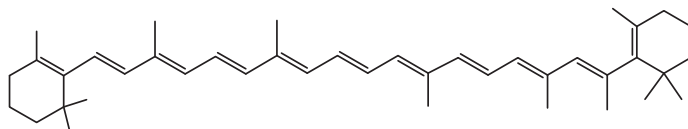
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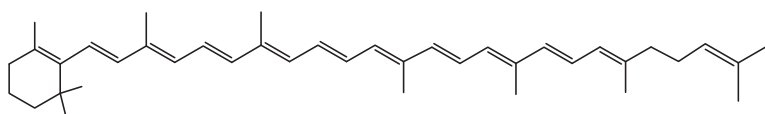
β-Carotene
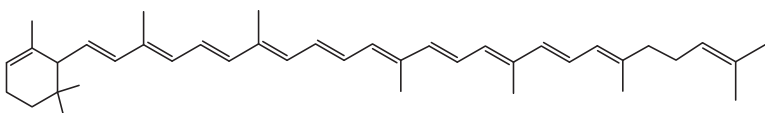
γ-Carotene

ε-Carotene
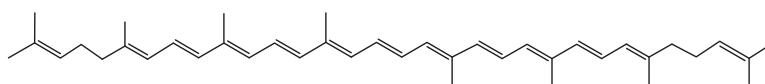
Lycopene

Polyenes group (**II**)

The alternative double bonds and conjugation in the polyenes are one of the main properties of these compounds. Some of properties that can be computed using the molecular orbital methods are λ_{max} and the difference energy level of the HOMO and LUMO orbitals (ΔE). For calculation of the λ_{max} of compounds **(I)** and **(II)**, we utilised the 'Fiser–Kuhn rule' (see Equation (7) [30]).

2. Mathematical methods

The branching index that was introduced by *Randić* is defined as the sum of certain bond contributions, calculated from the degree of the bonds, representing suppressed molecular graphs. These bond contributions, named C_{ij} are calculated as:

$$C_{ij} = (\delta_i \delta_j)^{-0.5}, \tag{1}$$

where δ_i is the degree of the vertex representing atom '*i*', i.e. the number of bonds incident to this atom. Accordingly, the *Randić* index is defined as [1,7,31,32]:

$$\chi = \sum C_{ij} = \sum (\delta_i \delta_j)^{-0.5}, \tag{2}$$

where the summation is carried out over all the bonds of linear simply conjugated polyenes (I). The inverse squared-root of the vertex degree is identified here as a measure of the relative accessible perimeter of an atom from the outside. These perimeters, which have units of length, are proposed to be measured in a new unit called the *Randić* index (χ). On this basis, the bond contributions to the *Randić* index are relative areas of bond accessibility from the environment.

For the two ends of the polyene chains **I**, the *Randić* indices are: $C_1 = C_n = 1/(2 \times 3)^{0.5}$ (only for ethylene: $C_1 = C_n = 1/(2 \times 2)^{0.5}$). For each carbon atom between the head and tail in the polyene chains, **I**, the *Randić* indices are: $C_2 = Cn_{x-1} = 1/(3 \times 3)^{0.5}$. On this basis, the final equation for calculating the *Randić* indices of the linear simple conjugated polyenes (**I**) is:

$$\chi = 2\left[\frac{1}{(2 \times 3)^{0.5}}\right] + \left[\frac{(N_B - 2)}{(3 \times 3)^{0.5}}\right] \tag{3}$$

and:

$$\chi = 2\left[\frac{1}{(6)^{0.5}}\right] + \left[\frac{(A - 3)}{3}\right], \tag{4}$$

where A is the number of conjugated carbon atoms and N_B is the number of atoms whose *Randić* indices are $1/(3 \times 3)^{0.5}$ in the compounds **I**.

If n_0 is equal to $A - 3$ ($n_0 = A - 3$), the number of nodes in the HOMO orbital of the linear simple conjugated polyenes (**I**) is obtained as follows:

$$\chi = 0.82 + [0.33(A - 3)], \tag{5}$$

$$\chi = 0.82 + [0.33(n_0)]. \tag{6}$$

For calculating the λ_{max} of polyenes **I**, the Fieser–Kuhn rule was first used Equation (7). These maximum wavelengths (λ_{max}) are calculated as:

$$\lambda_{max} = 114 + 5M + n_x(48.0 - 1.7n_x) - 16.5R_{endo} - 10R_{exo}, \tag{7}$$

where M is the number of alkyl substitution (equal to zero in **I** and structure dependent in **II**), n_x is the number of conjugated double bonds, R_{endo} is the number of 'endo' double bonds (equal to zero in **I** and structure dependent in **II**), and R_{exo} is the number of 'exo' double bonds (equal to zero in **I** and structure dependent in **II**). Thus, the final equation of Fieser–Kuhn rule for group **I** is:

$$\lambda_{max} = 114 + n_x(48.0 - 1.7n_x). \tag{8}$$

If $A = 2n_x$ (A = The number of conjugated atoms in **I**), then:

$$\lambda_{max} = 114 + \frac{A}{2}\left[48.0 - A\left(\frac{1.7}{2}\right)\right], \tag{9}$$

$$\lambda_{max} = 114 + A\left[\frac{(48.0 - 0.85A)}{2}\right]. \tag{10}$$

Table 1. The values of the relative structural coefficients of polyenes **(I)**.

No.	Compounds	n_x	A	*Randić* index (χ)	Log (χ)	λ_{max} (nm)	ΔE (in Joul $\times 10^{-19}$)	Log K_{ow}	$TB_d \times 10^{-4}$ (mol h^{-1})
1	C_4H_6	1	4	1.56	0.1931	203.2	9.78	2.0330	0.38
2	C_6H_8	2	6	2.13	0.3483	242.7	8.18	2.8002	0.36
3	C_8H_{10}	3	8	2.89	0.4609	278.8	7.13	3.5674	0.62
4	$C_{10}H_{12}$	4	10	3.46	0.5514	311.5	6.38	4.3346	1.7
5	$C_{12}H_{14}$	5	12	4.13	0.6263	340.8	5.83	5.1018	3.6
6	$C_{14}H_{16}$	6	14	4.89	0.6893	366.7	5.42	5.8690	4.1
7	$C_{16}H_{18}$	7	16	5.56	0.7451	389.2	5.10	6.6362	3.7
8	$C_{18}H_{20}$	8	18	6.13	0.7945	408.3	4.87	7.4034	3.3
9	$C_{20}H_{22}$	9	20	6.89	0.8382	424.0	4.69	8.1706	3.0
10	$C_{22}H_{24}$	10	22	7.56	0.8785	436.3	4.55	8.9378	2.7
11	$C_{24}H_{26}$	11	24	8.13	0.9154	445.2	4.46	9.7050	2.5
12	$C_{26}H_{28}$	12	26	8.89	0.9489	450.7	4.41	10.4722	2.3

Notes: n_x = The number of conjugated double bonds. A = The number of conjugated atoms.

For group **II**, making substitutions into Equation (7) and using that $A = 2n_x$ results in Equation (11):

$$\lambda_{max} = 114 + A\left[\frac{(48.0 - 0.85A)}{2}\right] - 16.5R_{endo} - 10R_{exo} + 5M. \tag{11}$$

For calculation of ΔE, we have utilised Planck's formula ($\Delta E = hc/\lambda_{max}$). The results of these calculations are shown in Table 1.

2.1. *Graphs*

All graphing operations were performed using the Microsoft Office Excel 2003 program. The data for octanol–water partitioning coefficients and total biodegradation (log K_{ow} and TB_d, respectively) were calculated with the EPI-suit v3.12 package [33]).

3. Discussion

It is reported and accepted that the toxicity properties of organic compounds can be predicted on the basis of the log K_{ow} [34]. The QSAR results hold true for quite a lot of organic compounds, including those most commonly used for toxicity testing, and follow this standard pattern [35]. Biodegradation is usually quantified by incubating a chemical compound in the presence of a degrader, and measuring factors like oxygen or CO_2. The biodegradation QSAR studies demonstrate that microbial biosensors are a viable alternative means of reporting on potential biotransformation. However, though few chemicals have been tested, large datasets for different chemicals are needed for QSAR modelling [36]. This study shows the structural relationship between the *Randić* index and λ_{max}, ΔE, log K_{ow}, and total biodegradation for polyenes of group **(I)**, as well as the extension of the results for Carotenes (group **II**) as some important chemicals with special properties, including antioxidant activity.

The values of the relative structural coefficients of the polyenes' *Randić* index (χ) to maximum UV wave length (λ_{max}) and ΔE (basis on the λ_{max}), logarithm of

Table 2. The values of the relative structural coefficients of carotenes **(II)**.

No.	Compounds	n_x	A	Randić index (χ)	λ_{max} (nm)	ΔE (in Joul $\times 10^{-19}$)	Log K_{ow}	$TB_d \times 10^{-4}$ (mol h^{-1})
1	α-Carotene	10	20	9.47	432.5	4.59	11.17 (17.49)*	3.41 (1.5)*
2	β-Carotene	11	22	10.39	452	4.40	12.22 (17.62)	0.70 (1.5)
3	γ-Carotene	11	22	10.22	449.8	4.42	12.03 (17.63)	1.64 (1.5)
4	ε-Carotene	10	20	9.69	449	4.43	11.42 (17.64)	3.21 (1.5)
5	Lycopene	11	22	10.15	474	4.19	11.97 (17.50)	1.88 (1.5)

Notes: n_x = The number of conjugated double bonds. A = The number of conjugated atoms. *The values in parentheses were calculated by EPI-suit v3.12 package.

octanol–water partitioning coefficients (log K_{ow}), and calculated total biodegradation (TB_d) in mol h^{-1} are shown in Tables 1 and 2 for groups **I** and **II**, respectively. The numbers shown in Table 1 have some mathematical structures. The table reveals the three numerical progressions apparent in the *Randić* indices. On this basis, the distance number of the *Randić* indices of $\{C_4H_6, C_{10}H_{12}, C_{16}H_{18}, C_{22}H_{24}\}$, $\{C_6H_8, C_{12}H_{18}, C_{18}H_{20}, C_{24}H_{26}\}$ and $\{C_8H_{10}, C_{14}H_{16}, C_{20}H_{22}, C_{26}H_{28}\}$ is two units of *Randić* index. The λ_{max} values increase and $\Delta E = hc/\lambda_{max}$ decrease with the *Randić* values of the polyenes **(I)**. The values of the calculated log K_{ow} of the polyenes **(I)** increase with the number of conjugated double bonds. Instead of increasing in step with each C=C bond in the linear simple conjugated polyenes **(I)**, calculated log K_{ow} increased with a distance value equal to 0.7672. There no regular mathematical structure between the *Randić* index (χ), maximum UV wavelength (λ_{max}) or ΔE (based on the λ_{max}) with calculated total biodegradation (TB_d).

In Figures 1–5 the two-dimensional diagrams of the relationship between the values of the *Randić* index, λ_{max}, ΔE, log K_{ow} and TB_d are shown. In some figures, the logarithmic values of these amounts were demonstrated.

Figure 1 shows a good linear relationship between the values of log(K_{ow}) *versus* the *Randić* indices (χ) for polyenes **(I)**. Equation (12) relates to Figure 1, and, as can be seen by this equation, can extend the linear behaviour of the calculated log K_{ow} and χ for polyenes **(I)**. The *R*-squared value (R^2) for this graph is equal to 0.9996.

$$\log K_{ow} = 1.1475(\chi) + 0.3029. \tag{12}$$

By combining Equations (4) and (11), we arrive at Equation (13). This equation describes the correlation of λ_{max} with the *Randić* index (χ) for the linear simple conjugated polyene compounds **(I)**.

$$\lambda_{max} = 126.85 + 70.63(\chi) - 3.82(\chi)^2. \tag{13}$$

For polyenes of group **II**, we can also utilise Equation (13) to a very good approximation. Equation (15) is the result of some simple mathematical operations on Equation (12) combined into the result of Equation (14).

$$\lambda_{max} = 126.85 + 70.63\left[\frac{(\log(K_{ow}) - 0.3029)}{1.1475}\right] - 3.82\left[\frac{(\log(K_{ow}) - 0.3029)}{1.1475}\right]^2, \tag{14}$$
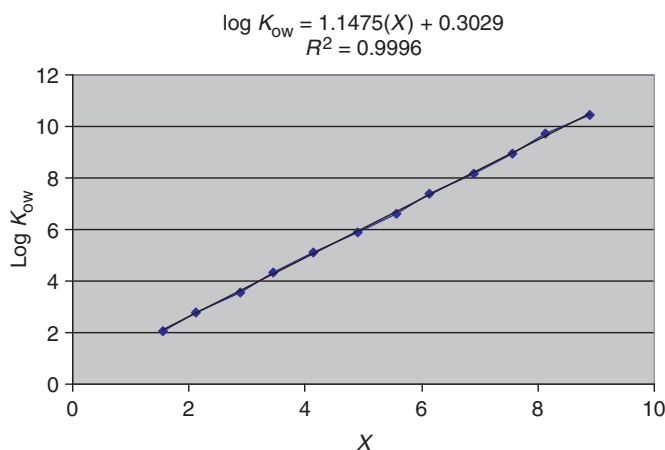
$$\log K_{\text{ow}} = 1.1475(X) + 0.3029$$
$$R^2 = 0.9996$$

Figure 1. The linear relationship between the values of log(K_{ow}) *vs.* the *Randić* indices (χ) for polyenes (**I**).

and:

$$2.901 \log(K_{\text{ow}})^2 - 62.01(\log(K_{\text{ow}}) + \lambda_{\max}) - 115.14 = 0. \tag{15}$$

In this way, Equations (12) and (15) afford a good approximation for calculating the logarithm value of the octanol–water partitioning coefficient (log K_{ow}) by using the *Randić* index (χ) and maximum UV wave length ($\lambda_{\max}$), directly. The large values resulting from solving the second-order Equation (15) are acceptable. The value of log K_{ow} can be obtained directly from Equation (12), in accordance with the structural χ values for these compounds.

Figures 2–4 show the plot of the log(K_{ow}) *versus* the log(χ), the curves of maximum UV wavelength ($\lambda_{\max}$) of polyenes (**I**) and the values of ΔE (HOMO-LUMO gap), respectively. With increasing number of double bonds in **I**, the values of log(K_{ow}), $\lambda_{\max}$ and log(χ) increase. Although perhaps not obvious from these figures, the relationship between the variables is decidedly non-linear, though this does not diminish their utility.

For the calculation of ΔE and the difference energy between HOMO and LUMO (ΔE in Joul $\times 10^{-19}$) for polyenes (**I**), one can simply use Planck's formula ($\Delta E = hc/\lambda_{\max}$). Figure 2 shows that by increasing the number of double bonds in **I**, the $\Delta E = hc/\lambda_{\max}$ decreased. Therefore, the values of the calculated log K_{ow} of the polyenes (**I**) increased with the number of conjugated double bonds, and decreased the energy gap between HOMO and LUMO (ΔE) for these compounds. Instead of increasing with each C=C bond in the linear simple conjugated polyenes (**I**), calculated log K_{ow} increased with the distance value equal to 0.7672. But the same steps and structural mathematics for ΔE *versus* log K_{ow} do not exist (see Figures 3 and 4).

Figure 3 shows a curve for the relationship between the values of calculated total biodegradation (TB_d) *versus* the *Randić* indices (χ) for polyenes (**I**). Equation (16) is relevant to Figure 5, and as can see by this equation, one can extend the linear behaviour of the calculated total biodegradation (TB_d) and χ for polyenes (**I**). The equation is sixth order. The R-squared value (R^2) for this graph shows 0.9618.

$$TB_d = -0.0071(\chi)^5 + 0.2121(\chi)^4 - 2.3693(\chi)^3 + 12.023(\chi)^2 - 26.144(\chi) + 19.877. \tag{16}$$
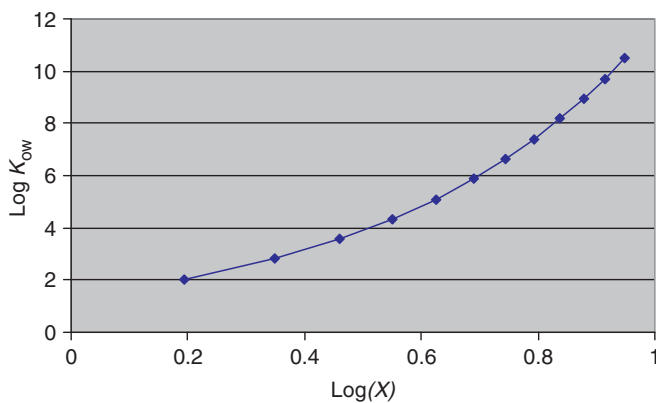
A.A. Taherpour et al.

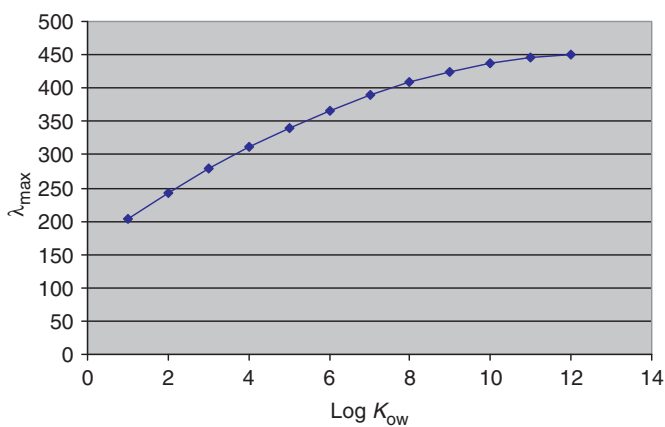Figure 2. A plot of the log(K_{ow}) *vs.* the log(χ) for polyenes **(I)**.

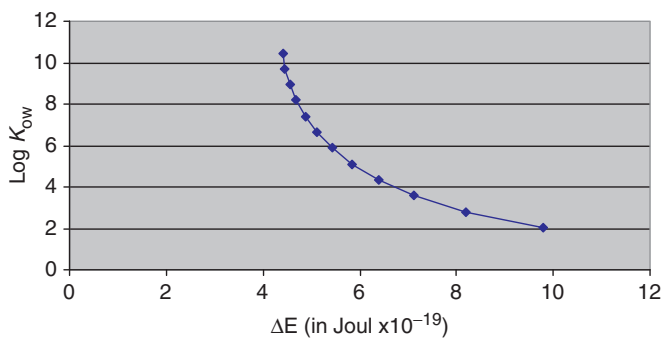Figure 3. The curve of the maximum UV wavelength (λ_{max}) of polyenes **(I)** and the values of log(K_{ow}).

Figure 4. A plot of the log(K_{ow}) *vs.* the difference level of HOMO and LUMO (ΔE in Joul $\times 10^{-19}$) for polyenes **(I)**.

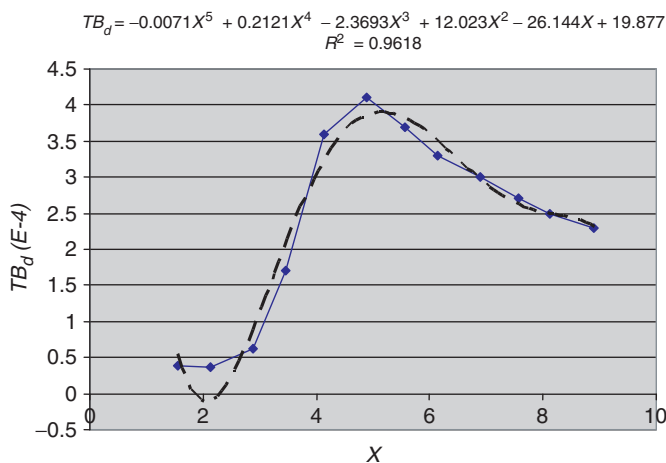$$TB_d = -0.0071X^5 + 0.2121X^4 - 2.3693X^3 + 12.023X^2 - 26.144X + 19.877$$
$$R^2 = 0.9618$$

Figure 5. A curve between values of *Randić* indices and calculated total biodegradation (TB_d) for **(I)**.

By the use of *Randić* indices (χ) for polyenes **(I)**, Equation (16) can achieve a good approximation for the total biodegradation (TB_d), and these results can be extended for natural polyenes like group **II**. All values of TB_d should be scaled by 10^{-4} for obtaining total biodegradation in moles per hour.

The values for logarithms of octanol–water partitioning coefficients and total biodegradation ($\log K_{ow}$ and TB_d, respectively) were calculated by Equations (12) and (16), for group **II**. There is a difference for these important values of carotene compounds like α-carotene, β-carotene, γ-carotene, ε-carotene and lycopene **(group-II)**. These comparisons show good correlation between structures, properties and activities. The differences of $\log K_{ow}$ and TB_d could be determined by the use of the calculated (Fieser–Kuhn rule) or experimental λ_{max} (measurement by UV-spectrum), and calculated *Randić* indices (χ) for carotene compounds **(group-II)**, as important pigments and antioxidant compounds. The difference amounts of TB_d, may reflect the kinetic stability of compounds in group **II**. The kinetic stability, or willingness to take part in chemical and biochemical reactions (like oxidation and biodegradations), relates to the energy gap between HOMO and LUMO. The decreasing of ΔE, or, in accordance with *Planck*'s formula ($\Delta E = hc/\lambda_{max}$), the increasing of λ_{max} values, of polyenes (both group **I** and **II**). As Table 2 demonstrates, α-carotene has a large value for ΔE (or low value for λ_{max}). According to the results, lycopene has the shortest distance between HOMO and LUMO, with ΔE and λ_{max} equal to 4.19(in Joul $\times 10^{-19}$) and 474 nm, respectively. The values of the calculated $\log K_{ow}$ of the polyenes **(II)** increase with the number of conjugated double bonds. The values of $\log K_{ow}$ exceed 11.5 for β-carotene, γ-carotene and lycopene, with 11 conjugated C=C bonds. The values of Table 2 that are in parentheses were calculated by the EPI-suit v3.12 package. There is not any experimental data of $\log K_{ow}$ or TB_d available for this family of compounds. Following a decrease of one C=C bond in α-carotene and ε-carotene, in comparison with β-carotene, γ-carotene, and lycopene, the calculated $\log K_{ow}$ decreased below 11.5. There is not any regular mathematical structure between the *Randić* index (χ), maximum UV wavelength (λ_{max}), or ΔE (based on the λ_{max}) with calculated total biodegradation (TB_d). The values of the *Randić* indices (χ) for β-carotene, γ-carotene,

and lycopene with 11 conjugated double bonds is higher than that of α-carotene and ε-carotene with 10 conjugated double bonds. The value of total biodegradation (TB_d) calculated with EPI-suit v3.12 package is equal to 1.5×10^{-4} mol h^{-1}. The calculated values of total biodegradation for carotenes (group **II**) show noticeable differences by using the relationship with *Randić* indices (χ). The amounts of TB_d, are 3.41×10^{-4} and 3.21×10^{-4} mol h^{-1} for α-carotene and ε-carotene, respectively, with 10 conjugated double bonds, according to Equation (16). The values of TB_d are 0.7×10^{-4}, 1.64×10^{-4}, and 1.88×10^{-4} mol h^{-1} for β-carotene, γ-carotene, and lycopene with 11 conjugated double bonds, respectively. The differences in properties and activities for this group are related to the purely structural factors that were considered in this structural relationship. The *Randić* indices (χ) show good differences between the values of $\log K_{ow}$ and TB_d as two important factors in chemical and biochemical studies of these compounds.

4. Conclusion

Graph theory has been found to be an effective tool in QSAR and QSPR. A survey of the different useful applications of graph theory shows obviously that this area is an exploration of techniques in discrete mathematics, and its results can be applied in various fields of sciences. TIs contain valuable structural information as evidenced by the success of their widespread applications in QSAR. One of the useful indices for examination of structure–property relationships is the *Randić* index. The toxicity properties of organic compounds can be predicted on the basis of their $\log K_{ow}$. The biodegradation QSAR studies demonstrate that microbial biosensors are a viable alternative means of reporting on potential biotransformation. In this study, we considered the relationship of the *Randić* indices, the logarithm of calculated octanol–water partitioning coefficients, and total biodegradation ($\log K_{ow}$ and TB_d (mol h^{-1}), respectively) with λ_{max} and ΔE ($\Delta E = hc/\lambda_{max}$) for the linear simple conjugated polyenes (group-**I**).The results were extended for some of the carotene compounds (group-**II**). *Randić* indices (χ) show a good difference between the values of $\log K_{ow}$ and TB_d as two important factors in chemical and biochemical studies of these compounds.

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