Asian Journal of Chemistry Vol. 20, No. 1 (2008), 218-224

QSAR Study Between LC_{50} of Linear Simple Conjugated Polyene Compounds in Fish and UV Maximum Wave Length by the Use of Randic Index

AVAT (ARMAN) TAHERPOUR*†, AREZOU TAHERPOUR‡ and OMID TAHERPOUR‡‡
Department of Chemistry, Graduate School, Islamic Azad University
Arak Branch, P.O. Box 38135-567, Arak, Iran
E-mail: a.taherpour@uq.edu.au

In this study, the relationship is demonstrated between the Randic index and the calculated scales of LC_{50} in 96 h for fish by the use of EPI-suit v3.12 package, with maximum UV wavelength (λ_{max}) for the linear simple conjugated polyenes. The interesting results of concerning among these calculated scales of LC_{50}, λ_{max} and the Randic index for this compounds are presented. It seems that these results can use in environmental and chemical laboratory of veterinary studies.

Key Words: Molecular topology, Randic index, LC_{50}, Maximum UV wavelength, Polyenes, Chemical laboratory veterinary.

INTRODUCTION

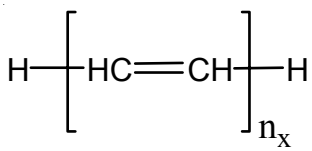
Graph theory has been found to be an effective tool in quantitative structure activity relationship (QSAR) and quantitative structure property relationship (QSPR)[1-8]. Topological indices are the numerical value associated with chemical constitution purporting for correlation of chemical structure with various physical properties, chemical reactivity or biological activity. Quantitative structural relationship studies are one of the main area of molecular topology and the results have applications in many areas of sciences such as studies of chemical properties in medicinal and pharmaceutical in veterinary studies area. A superior stages of topological indices (TI) started when Randic introduced the molecular branching index[7]. In 1975, Randic[7] proposed a topological index that has become one of the most widely used in both quantitative structure activity relationship and quantitative structure property relationship studies. These methods

†Present Address: Unusual Molecules & Reactive Intermediates Group, School of Molecular and Microbial Science, Chemistry Building, The University of Queensland, Brisbane-Qld 4072, Australia.

‡Medicinal Microbiology Department, Medicinal University of Kurdistan, Pasdaran Ave, Post Code: 66177-13446, Sonandaj, Kurdistan, Iran

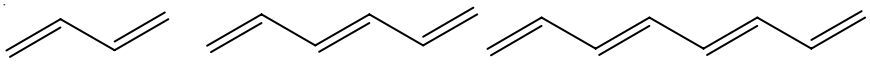
‡‡Veterinary Faculty, Islamic Azad University, Karaj Branch, Karaj, Iran.

prepared mathematical models designed for the correlation of various types of biological activity, chemical reactivity, equilibria, physical and physicochemical properties with electronic, steric, hydrophobic and other factors of a molecular structure of a given series of compounds such as substituent constants, topological indices (TI) as well as with solvent and other physicochemical parameters. An LC_{50} value is the concentration of a material in air that will kill 50 % of the test subjects (animals, typically mice or rats) when administered as a single exposure (typically 1 or 4 h). Also called the median lethal concentration and lethal concentration 50, this value gives an idea of the relative acute toxicity of an inhalable material. Other variants that are occasionally used are the LC_{25} and LC_{75}, which refer to the lethal concentration that kills 25 and 75 % of test subjects, respectively. Both LC_{50} and LD_{50} values state the animal used in the test. This is important because animal toxicity studies do not necessarily extrapolate (extend) to humans. For example, dioxins are highly toxic to guinea pigs and ducklings at extremely low levels, but have never been conclusively linked to a single human death even at very high levels of acute (short term) exposure. However, it is best for the safe side when evaluating animal toxicity studies and assume that most chemicals that are toxic to animals are toxic to humans. Typical units for LC_{50} values are parts per million (ppm) of material in air, micrograms (10^{-6} = 0.000001 g) per liter of air and milligrams (10^{-3} = 0.001 g) per cubic meter of air[8-16]. There are two types of the fishes that were often considered in the more of veterinary studies: *Carassius auratus* (Gold fish) and *Perca fluviatilis* (the sea fish).



n_x = 1,2,3, …, 11

Polyenes group (I)



Buta-1,3-diene Hexa-1,3,5-triene Octa-1,3,5,7-tetraene

In this study, the relationship of Randic index (χ), the calculated scales of LC_{50} in 96 h for fish by the use of EPI-suit v3.12 package[17] will be considered with maximum UV wave length (λ_{max}) and ΔE ($\Delta E = hc/\lambda_{max}$) for the linear simple conjugated polyenes (group-I).

EXPERIMENTAL

The median lethal concentration or lethal concentration 50 (LC_{50}) were calculated by EPI-suit v3.12 package. The LC_{50} of the mixture is estimated using the formula:

$$LC_{50}(\text{mixture}) = \frac{1}{\sum_{i-1}^{n} \frac{f_i}{LC_{50_i}}} \quad (1)$$

where, f_i = mole fraction of the ith component substance of the liquid. LC_{50_i} = mean lethal concentration of the ith component substance in mL/m^3. But in this study each of the components was used as an individual compound and without using the interfere form[16].

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

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

where δ_i is the degree of the vertex representing atom 'i', *i.e.*, the number of bonds incident to this atom. Accordingly, the Randic index is defined as:[1,7,18,19]

$$\chi = \Sigma \, C_{ij} = \Sigma(\delta_i \, \delta_j)^{-0.5} \quad (3)$$

where the summation is carried out over all the bonds of linear simply conjugated polyenes (**I**). The inverse square-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 length units, are proposed to be measured in a new unit called the Randic index (χ). On this basis, the bond contributions to the Randic index are relative areas of bond accessibility from the environment. For two ends of polyene chains **I**, the Randic 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 the each carbon atoms between the head and tail in the polyene chains **I** the Randic indices are: $C_2 = Cn_{x-1} = 1/(3 \times 3)^{0.5}$. The quantitative structural relationship between the Randic indices and maximum UV wavelength (λ_{max}) and ΔE ($\Delta E = hc/\lambda_{max}$) for the linear simple conjugated polyenes was reported[20]. The eqn. 3 shows this relationship. This equation describes correlation of λ_{max} and Randic index (χ) for the linear simple conjugated polyene compounds (**I**).

$$\lambda_{max} = 126.85 + 70.63 \, (\chi) — 3.82 \, (\chi)^2 \quad (4)$$

Graphs: For drawing and some equations concern to the graphs was used the Microsoft Office Excel-2003 program. The data of the median lethal concentration or lethal concentration 50 (LC_{50}) were calculated by EPI-suit v3.12 package[17].

RESULTS AND DISCUSSION

The values of the relative structural coefficients of the linear simply conjugated polyenes (**I**), Randic index (χ) and the other related data were shown in Table-1. As the values shown in the table, the Randic indices increase with molecular size of polyenes (**I**). The Table-1 reveals the three numerical progression indicated in the Randic indices. On this basis, the distance number of the Randic 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 (2) units of Randic index. In Figs. 1-3, it is attempted to show two dimensional diagrams of the relationship between the main values of LC_{50}, χ and

TABLE-1
VALUES OF THE RELATIVE STRUCTURAL COEFFICIENTS OF POLYENES (**I**)

Compd.	n_x	A	Randic index (χ)	log (χ)	λ_{max} (nm)	ΔE (Joul $\times 10^{-19}$)	LC_{50} 96 (h) mg/L (ppm)
C_4H_6	1	4	1.56	0.1931	203.2	9.78	37.578
C_6H_8	2	6	2.13	0.3483	242.7	8.18	10.515
C_8H_{10}	3	8	2.89	0.4609	278.8	7.13	2.631
$C_{10}H_{12}$	4	10	3.46	0.5514	311.5	6.38	0.632
$C_{12}H_{14}$	5	12	4.13	0.6263	340.8	5.83	0.143
$C_{14}H_{16}$	6	14	4.89	0.6893	366.7	5.42	0.105
$C_{16}H_{18}$	7	16	5.56	0.7451	389.2	5.10	0.007
$C_{18}H_{20}$	8	18	6.13	0.7945	408.3	4.87	0.00147
$C_{20}H_{22}$	9	20	6.89	0.8382	424.0	4.69	30.8 E-5
$C_{22}H_{24}$	10	22	7.56	0.8785	436.3	4.55	6.40 E-5
$C_{24}H_{26}$	11	24	8.13	0.9154	445.2	4.46	1.34 E-5
$C_{26}H_{28}$	12	26	8.89	0.9489	450.7	4.41	2.76 E-6

n_x = The number of conjugated double bonds, A = The number of conjugated atoms.

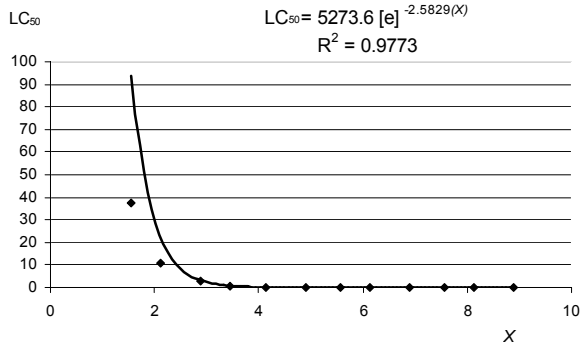


Fig. 1. A plot of the Randic indices (χ) *vs.* the LC_{50} 96 (h) mg/L (ppm) of simple linear polyenes (**I**)

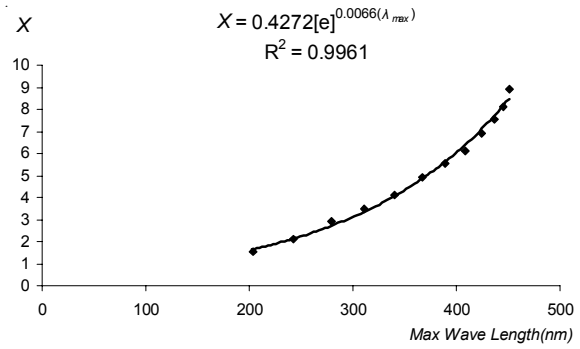


Fig. 2. A curve between values of Randic indices and values of the maximum UV wave length (λ_{max}) for (**I**)

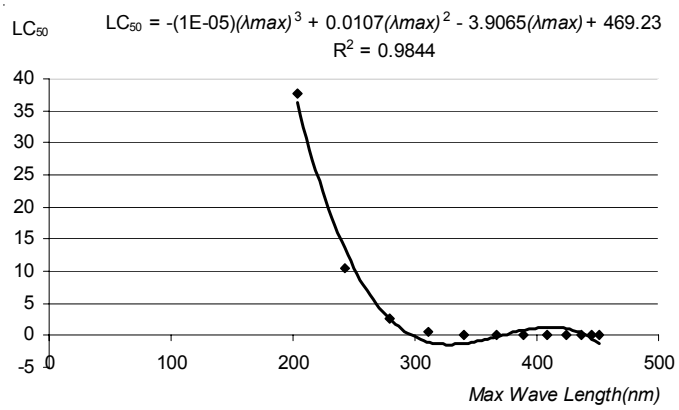


Fig. 3. The diagram of correlation between LC_{50} 96 (h) mg/L (ppm) and values of the maximum UV wave length (λ_{max}) for polyenes (**I**)

λ_{max} (Table-1). There are not any regular and simple mathematical structure between Randic index (χ), maximum UV wave length (λ_{max}) with LC_{50} (in ppm) of these compounds in fish. It seems that in lieu of increasing the C=C and Randic index in polyenes (**I**) the LC_{50} and λ_{max} shows decreasing in fish and in the condition of this study. It demonstrate that the ΔE (in Joul $\times 10^{-19}$) or HOMO-LUMO distance decreased and the kinetic stability comes down. On the other hand by increasing the reactivity willingness of polyenes (**I**) and decreasing the kinetic stability, the scales of the LC_{50} and λ_{max} shows decreasing in the condition of this study.

Fig. 1 shows a curve for relationship between the values of calculated LC_{50} *vs.* the Randic Indices (χ) for polyenes (**I**). The eqn. 5 is relevant to Fig. 1 and as could see by this equation can extend the behaviour of the

calculated lethal concentration 50 in 96 h mg/L (ppm) (LC_{50}) and χ for polyenes (**I**). The equation has a Nieperian structure with Randic indices (χ). The R-squared value (R^2) for this graph shows 0.9773.

$$LC_{50} = 5273.6 \exp [-2.5829(\chi)] \quad (5)$$

By this equation can use the of Randic indices (χ) for polyenes (**I**) to achieve a good approximation for LC_{50} and extend the results to other polyenes.

Fig. 2 demonstrated the relationship between 'χ' and the maximum UV wave length (λ_{max}). The eqn. 6 is the mathematical result of Fig. 2. In this figure can see a curve of the λ_{max} and χ for polyenes (**I**). This equation like eqn. 5 shows the Nieperian structure between these two quantities. The R-squared value (R^2) for this curve is 0.9961.

$$\chi = 0.4272 \exp [0.0066 (\lambda_{max})] \quad (6)$$

The relationship between the variables is non-linear, which however does not diminish their utility. The results in Fig. 3 demonstrated that a curve for relationship between the values of calculated lethal concentration 50 in 96 h mg/L (ppm) (LC_{50}) for fish and the maximum UV wave length (λ_{max}) for polyenes (**I**). The equation has three-order structure. The R-squared value (R^2) for this graph shows 0.9844.

$$LC_{50} = -(10^{-5}) (\lambda_{max})^3 + 0.0107 (\lambda_{max})^2 - 3.9065 (\lambda_{max}) + 469.23 \quad (7)$$

By this equation and determination the experimental λ_{max} by the use of UV-spectrophotometer can measure the LC_{50} of these compounds in fish in 96 h mg/L (ppm). It seems that two methods were achieved for LC_{50} calculation of polyene compounds (**I**) in fish, for 96 h mg/L (ppm). One of these two models, is calculation of Randic indices (χ) for polyenes (**I**) by the use of eqn. 6, then use it in the eqn. 5. The second method is the measurement of λ_{max} by the use of UV-spectrophotometer or eqns. 3 and 4, then utilize the result in eqn. 7. These two methods show a good approximation for determining the lethal concentration or lethal concentration 50 (LC_{50}) of the linear simple conjugated polyene compounds (**I**) in fish, for 96 h mg/L (ppm).

Conclusion

The topological resonance of simple linear polyenes scheme rests on the formalism of graph theory. A characteristic polynomial is constructed for the reference structure with the graphs for the given molecule taken into account. The applications of graph theory has been found to be an effective tool in QSAR and QSPR. One of the useful indices for examination of structure-property relationship is Randic index. In this study, the relationship of Randic indeices, LC_{50} of these compounds in fish in 96 h mg/L (ppm) and the maximum UV wavelength (λ_{max}) of polyenes (**I**) has

been demonstrated. By increasing the reactivity willingness of polyenes (**I**) and decreasing the kinetic stability, the scales of the LC_{50} and λ_{max} shows decreasing in the condition of this study. Two methods that were achieved for LC_{50} calculation of polyene compounds (**I**) in fish, here, show a good approximation for determining the lethal concentration 50 (LC_{50}) of the linear simple conjugated polyene compounds (**I**) in fish, for 96 h mg/L (ppm).

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the colleagues in Reactive Intermediates and Unusual Molecules Group of Chemistry Department, School of Molecular and Microbial Science, The University of Queensland, Australia, for their useful suggestions.

REFERENCES

1. P.J. Hansen and P. Jurs, *J. Chem. Educ.*, **65**, 574 (1988) and the literature cited therein.
2. H. Hosoya, *Bull. Chem. Soc. (Japan)*, **44**, 2332 (1971).
3. M. Randic, *Acta Chim. Slov.*, **45**, 239 (1998).
4. G. Rücker and C. Rücker, *J. Chem. Inf. Comput. Sci.*, **39**, 788 (1999).
5. H. Wiener, *J. Am. Chem. Soc.*, **69**, 17 (1947).
6. Y.P. Du, Y.Z. Liang, B.Y. Li and C.J. Xu, *J. Chem. Inf. Cmput. Sci.*, **42**, 1128 (2002).
7. M. Randic, *J. Am. Chem. Soc.*, **97**, 6609 (1975).
8. M. Randic, D. Plavsic and N. Ler, *J. Chem. Inf. Comput. Sci.*, **41**, 657 (2001).
9. O. Ivanciuc, *Rev. Roum, Chim.*, **45**, 1027 (2000).
10. M. Randic, *J. Am. Chem. Soc.*, **97**, 6609 (1975).
11. L.B. Kier and L.H. Hall, Molecular Connectivity in Structure-Activity, Research Studies Press, Letchwork (1986).
12. I. Gutman and M. Randic, *Chem. Phys. Lett.*, **47**, 15 (1977).
13. L.B. Kiere, *Quant. Struc.-Act. Relat.*, **4**, 109 (1985).
14. A. Balaban, *Chem. Phys. Lett.*, **89**, 399 (1982).
15. H. Kubinyi, *Quant. Struct.-Act. Relat.*, **13**, 285 (1994).
16. http://www.ilpi.com/msds/ref/lc50.htmL.
17. L.B. Kier and L.H. Hall, *J. Chem. Inf. Comput. Sci.*, **40**, 729 (2000).

(*Received*: 16 September 2006; *Accepted*: 5 September 2007) AJC-5809