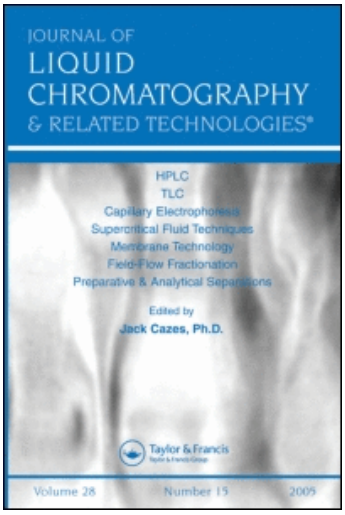


Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

THE APPLICATION OF TOPOLOGICAL INDEXES FOR PREDICTION OF THE R_M VALUES FOR TOCOPHEROLS IN RP-TLC

A. Pyka[a]; A. Niestrój[b]
[a] Faculty of Pharmacy, Academy of Medicine, Sosnowiec, Poland [b] Silesian University, Institute of Chemistry, Katowice, Poland

Online publication date: 30 September 2001

To cite this Article Pyka, A. and Niestrój, A.(2001) 'THE APPLICATION OF TOPOLOGICAL INDEXES FOR PREDICTION OF THE R_M VALUES FOR TOCOPHEROLS IN RP-TLC', Journal of Liquid Chromatography & Related Technologies, 24: 16, 2399 — 2413
To link to this Article: DOI: 10.1081/JLC-100105947
URL: http://dx.doi.org/10.1081/JLC-100105947

J. LIQ. CHROM. & REL. TECHNOL., 24(16), 2399–2413 (2001)

THE APPLICATION OF TOPOLOGICAL INDEXES FOR PREDICTION OF THE R_M VALUES FOR TOCOPHEROLS IN RP-TLC

A. Pyka[1,*] and A. Niestrój[2]

[1]Faculty of Pharmacy, Academy of Medicine,
4, Jagiellonska Street, PL-41-200 Sosnowiec, Poland
[2]Silesian University, Institute of Chemistry,
9 Szkolna Street, PL-40-006 Katowice, Poland

ABSTRACT

α-, β-, γ- and δ-tocopherols have been separated by reversed phase thin layer chromatography using seven different mobile phases. The R_M values of the compounds have been correlated with the numerical values of the topological indexes, the sum of the net electron charge (ΣNEC) on the tocopherols' –C-O-H groups, the moment dipoles (μ_{mph}), and the permitivities (ε_{mph}) of the mobile phases. Most accurate prediction of the R_M values of the tocopherols in all the mobile phases investigated, were achieved by use of two parametric equations employing the dipole moments of the mobile phases, and one topological index from among the topological indexes $^2\chi^v$, ^oB, C, or the sum of the net electron charge (ΣNEC).

*Corresponding author.

INTRODUCTION

One of the current tendencies in chemical investigations is the prediction of physicochemical and biological properties of chemical compounds from their structural parameters. The fundamental establishment of these investigations is the fact that the structure of a molecule determines its properties. This fact can be expressed by mathematical dependence(1,2)

$$P = f(S) \quad (1)$$

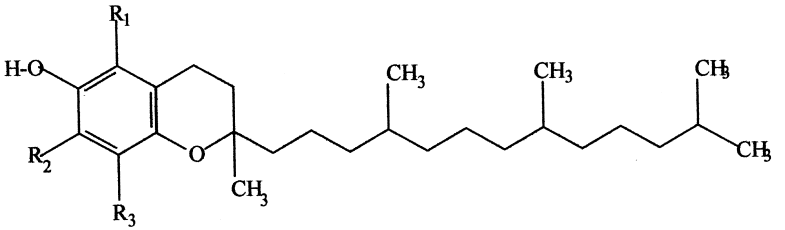
where: P is any physical, chemical, pharmacological, or toxicological property of a molecule, and S is any descriptor connecting with the structural aspects of a molecule.

Only the quantum mechanics completely describes the structure of a molecule characterizing her geometrical and electron structure. In many cases, the structural description of a molecule was shown by ways and order of a connection of atoms, and by form and size of a molecule. The topological indexes, which descend from a graph theory, are the simplest way to describe a structural description of a molecule. The topological indexes encode the structural information of a molecule. The topological index characterizes a molecule by a single number.(2,3) Characterizing a molecule by a single number represents a considerable loss of information. A three-dimensional object (compound) is described by a one-dimensional object (topological index).(3) The scientific literature describes more than 120 topological indexes (data from 1992 year).(3) Contemporaneously, the number of new topological indexes increases incessantly. The more important topological indexes were discussed in review.(3-9) From among all of the topological indexes, Randic ($^{0}\chi$, $^{1}\chi$, $^{2}\chi$, $^{0}\chi^{v}$, $^{1}\chi^{v}$, $^{2}\chi^{v}$), Gutman (M), Wiener (W), and Balaban (I_{β}) indexes are best described in respect to the applications. The applications of the topological indexes in the investigations: Quantitative Structure - Activity Relationships (QSAR), Quantitative Structure - Property Relationships (QSPR), and Quantitative Structure - Retention Relationships (QSRR) were described in scientific literature for organic compounds.(2,5-10)

Tocopherols are being intensively studied, owing to their medical, biological, and physico-chemical significance.(11-14) The problem of the separation of α-, β-, γ- and δ-tocopherols has been the subject of numerous papers.(15-17)

The aim of this work is the use of the topological indexes for prediction of the R_M values of the tocopherols separated by RP-TLC technique. The object of the investigations were: α-, β-, γ-, and δ-tocopherol, which the structures, the molecular weights; and the sum of the net electron charge (ΣNEC) on the tocopherol's –C-O-H groups are shown in Table 1.

Table 1. Structures, Molar Weights (M) of the Tocopherols Investigated, and the Net Electron Charge (ΣNEC) on the Compounds' –C-O-H Groups



Compound	R_1	R_2	R_3	M[g/mol]	ΣNEC [4]
DL-α-Tocopherol	$-CH_3$	$-CH_3$	$-CH_3$	430.71	0.0039
DL-β-Tocopherol	$-CH_3$	-H	$-CH_3$	416.68	0.0223
DL-γ-Tocopherol	-H	$-CH_3$	$-CH_3$	416.68	0.0327
DL-δ-Tocopherol	-H	-H	$-CH_3$	402.65	0.0432

EXPERIMENTAL METHODS AND CALCULATIONS

Chemicals

If not otherwise specified, all used chemicals (analytical grade), reference tocopherols, and HPTLC-solvents were from Merck, Darmstadt, Germany.

Sample Preparation

Commercial samples of α-, β-, γ-, and δ-tocopherol (#15496, E.Merck, Darmstadt, Germany) were used as test solutes: the aliquots of chloroform solutions of α-tocopherol (0.0233 M), β-tocopherol (0.024 M), γ-tocopherol (0.024 M), and δ-tocopherol (0.0249 M).

Separation of α, β, γ, and δ-Tocopherol by RP-HPTLC

RP-TLC was performed on 10 cm × 10 cm C_{18} reversed phase UV_{254} HPTLC plates (#1.13724, E. Merck, Darmstadt, Germany). A solution of mixture tocopherols was spotted on a chromatographic plate in quantities of 2 μL. Methanol, ethanol, n-propanol, and mixtures containing ethanol and water, and n-propanol and water in the volume proportions 9.5:0.5, and 9:1, were used as

mobile phases. The mobile phases were characterized by the dipole moments and the permitivities. The dipole moments (μ_{mph}) and the permitivities (ε_{mph}) of the mobile phases used were calculated from(18)

$$\mu_{mph}^2 = \sum_{i=1} N_i \mu_i^2 \quad (2)$$

$$\varepsilon = \sum_{i=1} V_i \varepsilon_i \quad (3)$$

where N_i and μ_i are the mass fraction and the dipole moment, and V_i and ε_i are the volume fraction and the permitivity, respectively, of the *i*th component of the mobile phase.

Chromatograms were visualized with a mixture of equal volumes of solutions of dipyridyl in methanol (0.5%) and ferric chloride in methanol (0.2%). The R_F values obtained counter average again on the R_M values according to formula:

$$R_M = \log\left(\frac{1}{R_F} - 1\right) \quad (4)$$

Calculation of Topological Indexes

The topological indices based on connectivity: Gutman (M),(4,8,9) and Randic ($^0\chi^v$, $^1\chi^v$, $^2\chi^v$),(4,6,8,9,19) on distance matrix: Wiener (W),(4,8,9,20) Pyka (^{0}B, C,D),(19,21) and Schultz (MTI - Molecular Topological Index),(4,22) were calculated for the investigated compounds. The Wiener, Pyka, and Schultz indices were calculated by building the distance matrix and determining its elements by means of values given by Barysz et al.(23)

The elements necessary for calculating of the topological indexes are presented in Table 2.

Table 2. The Elements Needed for Calculating of Topological Indexes

Valence Delta Values[8]		Diagonal Elements[23]			Off-Diagonal Elements[23]
Atom	δ^v	Atom	d_{ij}	Type of Bond	d_{ij}
-CH3	1	C	0	C – C	1.000
=CH2	2	O	0.25	C – O	0.750
≡CH	3			C = O	0.375
-OH	5			C – C_{arom}	0.667
=O	6				

RESULTS AND DISCUSSION

The mobile phases, their symbols, the numerical values of the dipole moments and the permitivities of these mobile phases, and the experimental R_M values obtained for each α-, β-, γ- and δ-tocopherol at use of these mobile phases are listed in Table 3.

These results indicate, that RP-TLC technique can be used to separating α-, β-, γ-, and δ-tocopherol. The R_M values of the tocopherols investigated grow smaller in following sequence:

α-tocopherol > β-tocopherol > γ-tocopherol > δ-tocopherol.

This dependence was observed in all applied mobile phases. In given sequence also will grow smaller hydrophobic properties of these tocopherols.

The topological indexes based on the connectivity: M, ${}^{o}\chi^{v}$, ${}^{1}\chi^{v}$, ${}^{2}\chi^{v}$, and on the distance matrix: W, ${}^{o}B$, C, D, and MTI are listed in Table 4.

The numerical values of the topological indexes: M, ${}^{o}\chi^{v}$, and ${}^{1}\chi^{v}$ grow smaller in following sequence:

α-tocopherol > β-tocopherol = γ-tocopherol > δ-tocopherol.

Table 3. R_M Values of Tocopherols and the Dipole Moments (μ_{mph}) and the Permittivities (ε_{mph}) of the Mobile Phases

Mobile Phase				R_M Values* of			
	Dipole Moment (μ_{mph}) [D]	Permittivities (ε_{mph})	Symbol of Mobile Phase	α-Tocopherol	β-Tocopherol	γ-Tocopherol	δ-Tocopherol
Methanol	1.6998	32.62	I	0.661	0.565	0.520	0.477
Ethanol	1.6489	24.55	II	0.017	−0.054	−0.124	−0.237
n-Propanol	1.5799	20.44	III	−0.589	−0.653	−0.723	−0.803
Ethanol+water 9.5:0.5, V/V	1.6625	27.24	IV	0.314	0.226	0.154	0.050
Ethanol+water 9.0:1.0, V/V	1.6757	29.93	V	0.647	0.591	0.540	0.489
n-Propanol +water 9.5:0.5, V/V	1.5982	23.34	VI	−0.466	−0.489	−0.512	−0.537
n-Propanol +water 9.0:1.0, V/V	1.6158	26.23	VII	−0.265	−0.302	−0.337	−0.414

*Average of 10 measurements.

Table 4. Numerical Values of the Topological Indexes M, $^{o}\chi^{v}$, $^{1}\chi^{v}$, $^{2}\chi^{v}$, W, ^{o}B, C, D, and MTI

	Topological Indexes								
	Gutman Index	Randić Indexes			Wiener Index	Pyka Indexes			Schultz Index
Tocopherol	M	$^{o}\chi^{v}$	$^{1}\chi^{v}$	$^{2}\chi^{v}$	W	^{o}B	C	D	MTI
α-	252	21.8657	13.0432	11.4415	3165.14	2.2070	25.251	190.30	15433.13
β-	244	20.9430	12.6205	11.0555	2944.79	2.1769	24.067	180.43	14554.13
γ-	244	20.9430	12.6205	11.0441	2946.00	2.1764	24.036	180.38	14560.14
δ-	236	20.0204	12.1979	10.6611	2728.94	2.1479	22.899	170.57	13692.47

These indexes have identical numerical values for β- and γ- tocopherol. It results from fact, that β- and γ- tocopherol are isomers.

Instead the numerical values of the Wiener index (W) and of the Schultz index (MTI) grow smaller in following orders:

α-tocopherol > γ-tocopherol > β-tocopherol > δ-tocopherol.

Only the numerical values of the topological indexes $^{2}\chi^{v}$, ^{o}B, C, and D decrease in given sequence:

α-tocopherol > β-tocopherol > γ-tocopherol > δ-tocopherol.

The sequence of these changes is consistent with the sequence of the changes of the R_M value of the tocopherols investigated. This is because these indexes have greatest meaning in prediction of the R_M value of the tocopherols investigated.

The correlation matrix for the $R_{M(all)}$ (for all measuring points – for all tocopherols investigated in all seven mobile phases, n=28), the sum of the net electron charge (ΣNEC) on the tocopherols' –C-O-H groups, the topological indexes values, and the dipole moments (μ_{mph}) and the permitivities (ε_{mph}) of the mobile phases, are listed in Table 5.

All correlation calculations were executed with the use of the Statgraphics computer program. The correlation coefficients counted indicate, that the $R_{M(all)}$ values cannot be predicted on the ground of no topological index and of the sum of the net electron charge (ΣNEC).

The significant linear relationships between the $R_{M(all)}$ values and the dipole moments, and the permitivities of mobile phases applied for the tocopherols investigated, were stated. However, the $R_{M(all)}$ values counted from such correlation equation will have these single numerical values for α-, β-, γ-, and δ-toco-

Table 5. Correlation Matrix* for the R_M, the Sum of the Net Electron Charge (ΣNEC) on the Compounds' –C-O-H Groups, Topological Indexes Values, and the Dipole Moments (μ_{mph}) and the Permittivities (ε_{mph}) of the Mobile Phases

	$R_{M(all)}$	ΣNEC	M	$^{o}\chi^{v}$	$^{1}\chi^{v}$	$^{2}\chi^{v}$	W	^{o}B	C	D	MTI	μ_{mph}	ε_{mph}
$R_{M(all)}$	1	−0.1457	0.1420	0.1420	0.1420	0.1426	0.1416	0.1423	0.1425	0.1421	0.1419	0.9627	0.8865
ΣNEC		1	−0.9577	−0.9577	−0.9677	−0.9617	−0.9577	0.9623	−0.9628	−0.9587	−0.9574	0	0
M			1	1	1	0.9999	1	0.9998	0.9998	1	1	0	0
$^{0}\chi^{v}$				1	1	0.9999	1	0.9998	0.9998	1	1	0	0
$^{1}\chi^{v}$					1	0.9999	1	0.9998	0.9998	1	1	0	0
$^{2}\chi^{v}$						1	0.9998	0.9998	0.9999	0.9999	0.9998	0	0
W							1	0.9998	0.9998	1	1	−0.0002	−0.0002
^{o}B								1	1	0.9998	0.9998	0	0
C									1	0.9998	0.9998	0	0
D										1	1	0	0
MTI											1	0	0
μ_{mph}												1	0.8633
ε_{mph}													1

* Correlation coefficient was calculated for all measuring points, n=28.

pherol within each of the mobile phases applied. The dipole moments and the permitivities characterize and differentiate each mobile phase. This is because to correlate equations it is necessary to introduce the parameter differentiating each tocopherol investigated. Such parameters can be the topological indexes and the sum of the net electron charge (ΣNEC).

With regard to the existing intercorrelation between single topological indexes and the sum of the net electron charge (ΣNEC) in the correlation equations, they can only be used alone. Instead, between the dipole moments (or the permitivities) and the topological indexes, there is no intercorrelation with ΣNEC. (Table 5). However, it is advisable to use such structural parameters (S) differentiating tocopherols as $^{2}\chi^{v}$, ^{o}B, C, D, and ΣNEC. This is because only these parameters change in proportion to changes in the experimental R_M values. The following dependences: $R_M = f(\mu_{mph}, S)$ and $R_M = f(\varepsilon_{mph}, S)$ were examined in four groups. Namely for:

1) the $R_{M(all)}$ values of the tocopherols investigated using all applied mobile phases (I-VII);

2) the $R_{M(mix)}$ values of the tocopherols investigated at use of methanol, ethanol and n-propanol as the mobile phases (I-III);

3) the $R_{M(et)}$ values of the tocopherols investigated at use of ethanolic mobile phases (II, IV, and V);

4) the $R_{M(pr)}$ values of the tocopherols investigated at use of propanolic mobile phases(III, VI, and VII).

The best relationships of two parametric equations, were obtained with the use of the dipole moments of the mobile phases and one from the structural parameters: $^{2}\chi^{v}$, ^{o}B, C, and ΣNEC. Analogously, the correlation equations taking into account the permitivities of the mobile phases, instead of the dipole moments of the mobile phases, are not statistically significant. The best correlation equations obtained are presented in Table 6.

The worst correlation equations were ascertained for the relationships taking into account all measurement – points (the $R_{M(all)}$ values of the tocopherols from all mobile phases marked I-VII). However, the best correlation equations were obtained for prediction of the $R_{M(mix)}$ and the $R_{M(et)}$ values. All correlation equations listed in Table 6 are statistically significant. For all correlation equations, the P-value is less than 0. 0001. Since the P-value in the Anova table is less than 0.01, there is a statistically significant relationship between the variables at the 99% confidence level. The high coefficients of determination (**R^2**), value of the Fisher test (**F**), small values of standard error of the estimate (**s**), and significance levels (**P**) of the equations presented in this Table 6 are indicative of the special physicochemical importance of the topological indexes and the sum of the net electron charge (ΣNEC). For example, the relationships between the R_M values measured experimentally and values calculated by use of eqs. (6), (10), (14), and (18) are shown in Figure 1.

Table 6. The Characteristics of the Multiple Correlation Equations Which Enable Prediction of the R_M Values of the Tocopherols Investigated

Eq. No	Equation	Statistical Data*			
		R^2	F	s	n
5	$R_{M(all)} = -21.0889(\pm1.2314) + 11.1984(\pm0.5350)\mu_{mph} + 0.2424(\pm0.0782)^2\chi^v$	94.71	223.9	0.114	28
6	$R_{M(all)} = -25.3626(\pm2.4142) + 11.1984(\pm0.5350)\mu_{mph} + 3.1933(\pm1.0329)^oB$	94.70	223.5	0.114	28
7	$R_{M(all)} = -20.3442(\pm1.0772) + 11.1984(\pm0.5350)\mu_{mph} + 0.08036(\pm0.02594)C$	94.71	223.8	0.114	28
8	$R_{M(all)} = -18.2904(\pm0.8710) + 11.1984(\pm0.5350)\mu_{mph} - 4.7097(\pm1.4742)\Sigma NEC$	94.80	227.9	0.113	28
9	$R_{M(mix)} = -20.0929(\pm1.1171) + 10.3020(\pm0.4357)\mu_{mph} + 0.2796(\pm0.0776)^2\chi^v$	98.45	286.0	0.074	12
10	$R_{M(mix)} = -25.0241(\pm2.3488) + 10.3020(\pm0.4369)\mu_{mph} + 3.6842(\pm1.0272)^oB$	98.44	284.4	0.074	12
11	$R_{M(mix)} = -19.2342(\pm0.9476) + 10.3020(\pm0.4360)\mu_{mph} + 0.09271(\pm0.02576)C$	98.45	285.5	0.074	12
12	$R_{M(mix)} = -16.8643(\pm0.6907) + 10.3020(\pm0.4197)\mu_{mph} - 5.4494(\pm1.4213)\Sigma NEC$	98.56	308.7	0.071	12
13	$R_{M(et)} = -44.3992(\pm1.9426) + 24.8429(\pm1.1300)\mu_{mph} + 0.3005(\pm0.0448)^2\chi^v$	98.32	264.2	0.043	12
14	$R_{M(et)} = -49.6973(\pm2.3031) + 24.8429(\pm1.1426)\mu_{mph} + 3.9591(\pm0.5928)^oB$	98.29	258.2	0.043	12
15	$R_{M(et)} = -43.4756(\pm1.9198) + 24.8429(\pm1.1344)\mu_{mph} + 0.09963(\pm0.01492)C$	98.31	262.1	0.043	12
16	$R_{M(et)} = -40.9293(\pm1.6809) + 24.8429(\pm1.0111)\mu_{mph} - 5.8291(\pm0.7625)\Sigma NEC$	98.66	331.1	0.038	12
17	$R_{M(pr)} = -18.7029(\pm1.0469) + 10.0997(\pm0.6149)\mu_{mph} + 0.1861(\pm0.0327)^2\chi^v$	97.11	151.1	0.031	12
18	$R_{M(pr)} = -21.9769(\pm1.3759) + 10.0997(\pm0.6225)\mu_{mph} + 2.4484(\pm0.4366)^oB$	97.04	147.3	0.032	12
19	$R_{M(pr)} = -18.1299(\pm1.0224) + 10.0997(\pm0.6184)\mu_{mph} + 0.06164(\pm0.01090)C$	97.08	149.4	0.031	12
20	$R_{M(pr)} = -16.5548(\pm0.9254) + 10.0997(\pm0.5790)\mu_{mph} - 3.5946(\pm0.5850)\Sigma NEC$	97.44	171.0	0.029	12

* $P<0.0001$ for all equations.

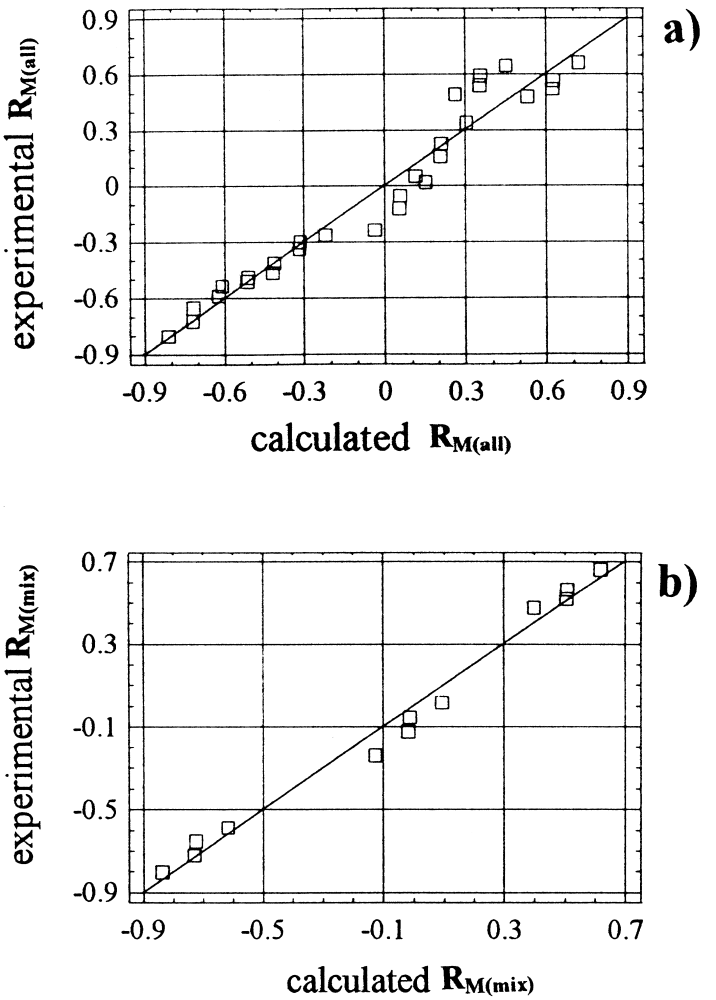


Figure 1. Relationships between the experimental R_M values of the α-, β-, γ-, and δ-tocopherols and the R_M values calculated by use of (**a**) eq.(6) (see Table 6), (**b**) eq.(10), (**c**) eq.(14), (**d**) eq.(18); where: the $R_{M(all)}$ values of the tocopherols with all mobile phases used (I-VII); the $R_{M(mix)}$ values of the tocopherols with methanol, ethanol, and n-propanol mobile phases used (I-III); the $R_{M(et)}$ values of the tocopherols with ethanolic mobile phases used (II, IV, and V); the $R_{M(pr)}$ values of the tocopherols with n-propanolic mobile phases used (III, VI, and VII).

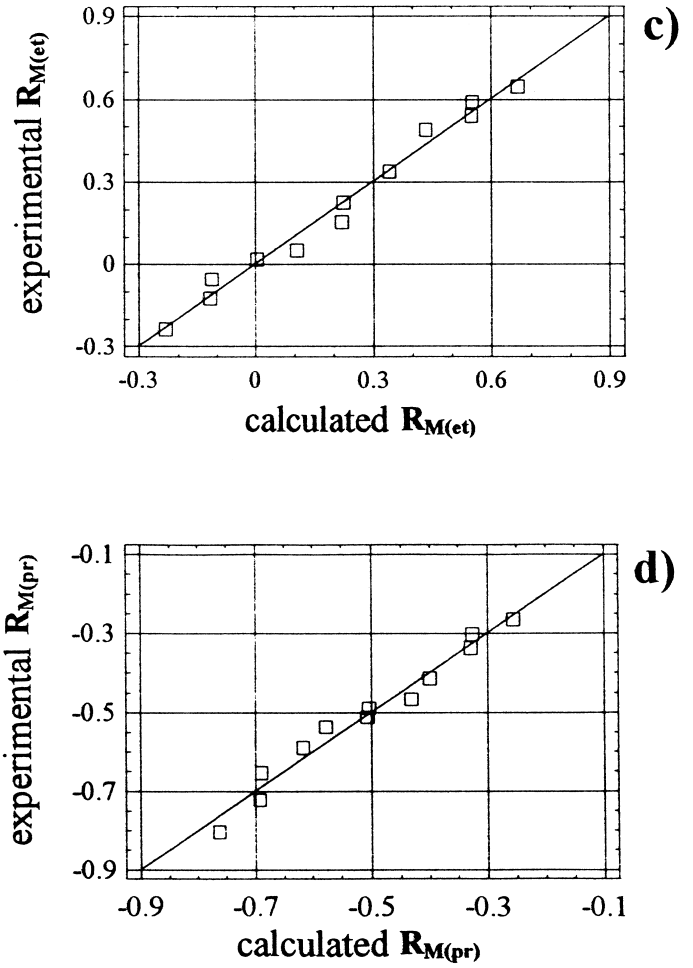


Figure 1. Continued.

The equations presented in Table 6 can also be used for the prediction of the R_M values of the tocopherols investigated, in which measurement points have not been taken into consideration in the equations. Several of the tests for predicting equations, like equations (6,10,13, and 17), are how well they predict values of points not included in the training set.

Four points (α-, β-, γ- and δ-tocopherols separated with VII mobile phase) were removed from the training set (eq.6), and the best sub-sets equation using two parameters were re-calculated as:

$$R_{M(all)} = -25.5480(\pm 2.8170) + 11.1631(\pm 0.6000)\mu_{mph} + 3.3062(\pm 1.2120)^{o}B$$
$$n = 24; \quad R^2 = 94.39\%; \quad F = 176.8; \quad s = 0.124; \quad P < 0.0001 \qquad (21)$$

Four points (α- and δ-tocopherols with VII mobile phase, β-tocopherol with IV mobile phase, and γ-tocopherol with III mobile phase) were removed from the training set (eq.6), and the best sub-sets equation using two parameters were re-calculated as:

$$R_{M(all)} = -25.5303(\pm 2.8309) + 11.1504(\pm 0.6214)\mu_{mph} + 3.3072(\pm 1.2123)^{o}B$$
$$n = 24; \quad R^2 = 94.01\%; \quad F = 164.7; \quad s = 0.124; \quad P < 0.0001 \qquad (22)$$

Table 7 gives the $R_{M(all)}$ values, experimental and predicted, from eqs. (21 and 22), of four points deleted from the training set.

Next, γ-tocopherol with III mobile phase (n-propanol) was removed from eq.(10), and the best sub-sets equation using two parameters were re-calculated as:

$$R_{M(mix)} = -25.0576(\pm 2.5144) + 10.3206(\pm 0.5022)\mu_{mph} + 3.6853(\pm 1.0890)^{o}B$$
$$n = 11; \quad R^2 = 98.18\%; \quad F = 216.6; \quad s = 0.079; \quad P < 0.0001 \qquad (23)$$

Next, β-tocopherol with IV mobile phase (ethanol+water, 9.5+0.5,V/V) was removed from eq.(13), and the best sub-sets equation using two parameters were re-calculated as:

$$R_{M(et)} = -44.3990(\pm 2.0604) + 24.8427(\pm 1.1985)\mu_{mph} + 0.3005(\pm 0.0475)^{2}\chi^{v}$$
$$n = 11; \quad R^2 = 98.32\%; \quad F = 234.8; \quad s = 0.0454; \quad P < 0.0001 \qquad (24)$$

Next, γ-tocopherol with VI mobile phase (n-propanol=water, 9.5+0.5, V/V) was removed from eq.(17), and the best sub-sets equation using two parameters were re-calculated as:

Table 7. $R_{M(all)}$ Values of Tocopherols Omitted (Experimental) from Eqs. (21) and (22), and Predicted by These Equations

Tocopherol	Experimental[a]	$R_{M(all)}$ Predicted by Eq.21	$\lvert \Delta R_{M(al1)} \rvert$	Experimental[a]	$R_{M(all)}$ Predicted by Eq.22	$\lvert \Delta R_{M(al1)} \rvert$
α-	−0.265	−0.214	0.051	−0.265	−0.214	0.051
β-	−0.302	−0.313	0.012	0.226	0.207	0.019
γ-	−0.337	−0.315	0.022	−0.723	−0.716	0.007
δ-	−0.414	−0.409	0.005	−0.414	−0.410	0.004

[a]Explanations in section "Results and Discussion."

Table 8. $R_{M(all)}$ Values of Tocopherols Omitted (Experimental) from Eqs. (23), (24), and (25), and Predicted by These Equations

Tocopherol	Experimental[a]	$R_{M(mix)}$ Predicted by Eq.23	$\lvert \Delta R_{M(al1)} \rvert$	Experimental[a]	$R_{M(et)}$ Predicted by Eq.24	$\lvert \Delta R_{M(al1)} \rvert$	Experimental[a]	$R_{M(all)}$ Predicted by Eq.25	$\lvert \Delta R_{M(al1)} \rvert$
γ-	−0.731	−0.723	0.008	-	-	-	−0.512	−0.506	0.006
β-	-	-	-	0.226	0.224	0.002	-	-	-

[a]Explanations in section "Results and Discussion."

$$R_{M(pr)} = -18.7028(\pm 1.1082) + 10.1003(\pm 0.6509)\mu_{mph} + 0.1860(\pm 0.0346)^{2}\chi^{v}$$
$$n = 11; \quad R^2 = 97.12\%; \quad F = 134.9; \quad s = 0.033; \quad P < 0.0001 \qquad (25)$$

Table 8 gives the $R_{M(mix)}$, $R_{M(et)}$, and $R_{M(pr)}$ values, experimental and predicted, from eqs. (23, 24, and 25) of the one point deleted from the training set.

The equations introduced can be of service for prediction of the R_M values of the tocopherols investigated, which were removed from the correlation equations. It was ascertained that, the differences in the numerical values among the topological indexes for the isomeric β- and γ-tocopherol are very little. It causes the R_M values counted for the β- and γ-tocopherol to differ imperceptibly between itself. However, it was shown (the $R_{M(all)}$ values predicted from equation 21 – Table 7) that, the sequence of the R_M values predicted on the ground of correlation equations is identical with the sequence of the experimental R_M values for the α-, β-, γ-, and δ-tocopherol. Future investigations will be concentrated on the research of new structural parameters (topological index), which will better differentiate the isomeric β- and γ-tocopherol.

ACKNOWLEDGMENTS

The authors wish to thank Prof. Dr. J. Sliwiok from the Institute of Chemistry, Silesian University, Katowice, Poland for donating the samples of the tocopherols used in our experiments, and also to Statgraphics for their computer program.

REFERENCES

1. Basak, S.C.; Monsrud, L.J.; Rosen, M.E.; Frane, C.M.; Magnuson, V.R. Acta Pharm. Jugosl. **1986**, *36*, 81-85.
2. Basak, S.C. Practical Applications of Quantitative Structure - Activity Relationships (QSAR). in *Environmental Chemistry and Toxicology*; Karcher, W.; Devillers, J., Eds.; ECSC, EEC, EAEC: Brussels, Luxembourg, 1990; 83-103.
3. Mihalic, Z.; Trinajstic, N. J. Chem. Educ. **1992**, *69*, 701-712.
4. Trinajstic, N. *Chemical Graph Theory*, CRC Press: Boca Raton, Florida, 1992.
5. Balaban, A.; Chiriac, A.; Motoc, I.; Simon, Z. *Steric Fit in Quantitative Structure - Activity Relations*; Springer Verlag: Berlin - Heidelberg - New York, 1980.
6. Kier, L.B.; Hall, L.H. *Molecular Connectivity in Structure-Activity Analysis*; Research Studies Press LTD: Letchworth, 1986.

7. Ekiert, L.; Bojarski, J.; Mokrosz, J.L. Wiad. Chem. **1986**, *40*, 65-83.
8. Balaban, A.T.; Motoc, I.; Bonchev, D.; Mekenyan, O. Top. Curr. Chem. **1988**, *114*, 21-55.
9. Pyka. A. Wiad. Chem. **1997**, *51*, 783-802.
10. *Topological Indices and Related Descriptors in QSAR and QSPR*; Devillers, J., Balaban, A.T., Eds.; Gordon and Breach Science Publishers: Amsterdam, 1999.
11. Davidek, J.; Janièek, G.; Pokorny, J. *Chemie Potravin*; ALFA, SNTL; Praha, 1983.
12. Sliwiok, J.; Kocjan, B. Fat Sci. Technol. **1992**, *94*, 157–189.
13. Beijersbergen van Henegouwen, G.M.J.; de Vries, H.; van den Broeke, L.T; Junginger, H.E. Fat Sci. Technol. **1992**, *94*, 24-27.
14. Leth, T.; Søndergaard, H. J. Nutr.**1977**, *107*, 2236-2243.
15. Rizzolo, A.; Polesello, S. J. Chromatogr. **1992**, *624*, 103-152.
16. Melchert, H.U.; Pabel, E. J. Chromatogr. A **2000**, *896*, 209-215.
17. Sliwiok, J.; Kocjan, B.; Labe, B.; Kozera, A.; Zalejska, J. J. Planar Chromatogr.-Mod. TLC **1993**, *6*, 492-494.
18. Minkin, V.J.; Osipov, O.V.; Zhdanov, A. *Momenty Dipolowe w Chemii Organicznej (Dipole Moments in Organic Chemistry)*, Warsaw, 1970.
19. Randic, M. J. Am. Chem. Soc. **1975**, *97*, 6609-6615.
20. Wiener, H. J. Am. Chem. Soc. **1947**, *69*, 2636-2638.
21. Pyka, A. J. Planar Chromatogr-Mod. TLC **1991**, *4*, 316-318.
22. Schultz, H.P. J. Chem. Inf. Comput. Sci. **1989***, 29*, 227-228.
23. Barysz, M.; Jashari, G.; Lall, R.S.; Srivastava, V.K.; Trinajstic, N. Chem. Appl. Topol. Graph Theory, Stud. Phys. Theoret. Chem. **1983**, *28*, 222-230.

Received March 28, 2001 Manuscript 5561
Accepted April 25, 2001