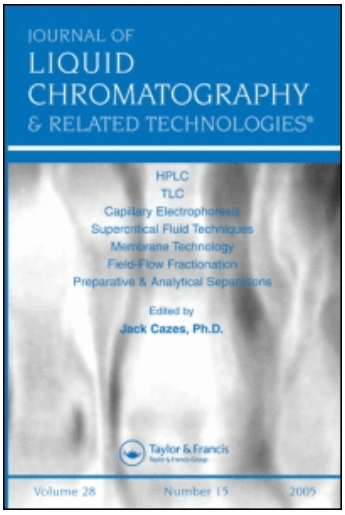

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INFLUENCE OF pH WATER ON THE LIPOPHILICITY OF NICOTINIC ACID AND ITS DERIVATIVES INVESTIGATED BY RP-TLC

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INFLUENCE OF pH WATER ON THE LIPOPHILICITY OF NICOTINIC ACID AND ITS DERIVATIVES INVESTIGATED BY RP-TLC

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□ *Nicotinic acid (1) and its derivatives, namely methyl nicotinate (2), ethyl nicotinate (3), isopropyl nicotinate (4), butyl nicotinate (5), hexyl nicotinate (6), benzyl nicotinate (7), nicotinamide (8), N-methylnicotinamide (9), N,N-diethylnicotinamide (10), 3-pyridinecarboaldehyde (11), 3-pyridinecarbonitrile (12), 3-pyridylmethanol (13), and methyl 3-pyridyl ketone (14) were investigated with the use reversed-phase thin layer chromatography on RP-2 plates (Kieselgel 60 F_{254} silanisiert, E. Merck), and methanol – water ($pH_{water} = 2.53$; 5.88; 8.11) in different volume compositions as a mobile phase. The chromatographic parameters of lipophilicity ($R_{MW(pH=2.53)}$; $R_{MW(pH=5.88)}$; $R_{MW(pH=8.11)}$) of the studied compounds were determined and compared with both measured ($logP_{exp}$), and calculated partition coefficients (AlogPs, IAlogP, ClogP, $logP_{Kowwin}$, xlogP, and miLogP). The lipophilicity R_{MW} values correlate well with experimental partition coefficients ($logP_{exp}$) for the compounds investigated. Best agreement was obtained with the experimental partition coefficients ($logP_{exp}$) and the chromatographic parameter of lipophilicity $R_{MW(pH=5.88)}$ for compounds investigated on RP-2 plates and by use of methanol + water ($pH_{water} = 5.88$) mobile phase. Chromatographic parameters of the lipophilicity correlated best with AlogPs. Moreover, ClogP correlated best with experimental partition coefficients ($logP_{exp}$) of the compounds studied.*

Keywords densitometry, experimental *n*-octanol-water partition coefficient, lipophilicity parameter R_{MW}, nicotinic acid, nicotinic acid derivative, RP-TLC, theoretical partition coefficient

INTRODUCTION

Lipophilicity is one of the parameters of chemical substances that influence their biological activities describing the beneficial or adverse effects of chemical substances (including drugs) on living matter. Lipophilicity is a prime parameter in describing both pharmacodynamic and pharmacokinetic aspects of drug action. The *n*-octanol-water partition

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coefficient is generally accepted as a useful parameter in structure activity relationship studies (QSAR) for the prediction of biological or pharmacological activity of compounds. The different partition chromatographic techniques and theoretical methods have been widely used as a reliable alternative to classical determination of logP. The investigations of relationships between the chromatographic parameter of lipophilicity R_{MW} and experimental ($logP_{exp}$), as well as theoretical partition coefficients calculated with the use of different computer programs (IAlogP, $logP_{Kowwin}$, ClogP, AlogPs, xlogP, miLogP, $logP_{Chem.Off}$, $logP_G$, logP (ACD/logP), logP (HyperChem), logP (ChemDraw)) of different groups of compounds, were the object of many scientific publications.[1–13] For example, significant correlation between the chromatographic parameter of lipophilicity R_{MW} and theoretical partition coefficient $logP_{Kowwin}$ was found for bile acids chromatographed on RP-18 W, RP-2, CN F_{254} plates using methanol + water, organic mixture + water, acetone + water, and dioxane + water mobile phases.[1,3–6] Good agreement with the chromatographic parameter of lipophilicity R_{MW} and experimental ($logP_{exp}$), as well as theoretical partition coefficients ClogP and IAlogP, was stated for steroid compounds chromatographed on RP-18 W plates using methanol + water and acetonitrile + water mobile phases.[7] The chromatographic parameter of lipophilicity R_{MW} correlated well with partition coefficients calculated with the use of computer programs, such as: ACD/logP, HyperChem and ChemDraw for series of synthesized potential antituberculotic compounds (substituted anilides of pyrazine-2-carboxylic acid) chromatographed on RP-2 plates using methanol + phosphate buffer at pH = 7.4 and 3.0 mobile phase.[8] Whereas, the chromatographic parameter of lipophilicity R_{MW} correlated poorly with partition coefficient $logP_G$ calculated with the use of ChemPlus software for another series of synthesized potential antituberculotic compounds (derivatives of 1,2,4-triazole and thiosemicarbazide) chromatographed on RP-18 W_{254} plates using methanol + water and acetonitrile + water mobile phases.[9] *N,N*-disubstituted-2-phenylacetamide derivatives were next group of compounds, of which the values of chromatographic parameter of lipophilicity R_{MW} were correlated with theoretical partition coefficients (logP) calculated with the use of different computer programs.[10] The compounds, aforementioned were chromatographed on RP-18 plates using binary mobile phases consisting of a mixture of water and one of the following organic modifiers: methanol, ethanol, 1-propanol, 2-propanol, acetonitrile, acetone, tetrahydrofurane, or dioxane. It was stated that there is a good linear correlation between the chromatographic parameter of lipophilicity R_{MW} and the theoretical partition coefficients AlogP, ClogP, miLogP, $logP_{Kowwin}$, xlogP, $logP_{ACD}$ and $logP_{Chem.Off}$.

In our earlier lipophilicity investigations of nicotinic acid, its esters, nicotinamide, and N-methylnicotinamide (9 compounds together) on

RP-18 F_{254} and RP-18WF_{254} plates using methanol + water as the mobile phase was estimated.[12,13] The most significant correlation was obtained between the chromatographic parameter of lipophilicity R_{MW} and the theoretical partition coefficient AlogPs. In this paper, the analyzed group of compounds was increased by *N,N*-diethylnicotinamide, 3-pyridinecarboaldehyde, 3-pyridinecarbonitrile, 3-pyridylmethanol, and methyl 3-pyridyl ketone (14 compounds together).

The aim of this study was to evaluate the influence of pH water on the lipophilicity of nicotinic acid and its derivatives by RP-TLC on RP-2 plates. The experimental *n*-octanol-water partition coefficients and chromatographic parameters of lipophilicity values were also compared with lipophilicity values estimated by computational methods for investigated compounds.

EXPERIMENTAL

Chemicals and Standard Solutions

The following components of the mobile phase: methanol (E. Merck, Germany; for liquid chromatography), and distilled water (pH = 5.88) were used for RP-TLC analysis. Distilled water was acidified with hydrochloric acid (35–38%, pure for analysis, POCh, Gliwice, Poland) to pH = 2.53, and alkalized with ammonia (25%, pure for analysis, POCh, Gliwice, Poland) to pH = 8.11. The pH of water was measured by use of pehameter (Elmetron, Poland). The commercial samples of nicotinic acid (1), methyl nicotinate (2), ethyl nicotinate (3), butyl nicotinate (5), nicotinamide (8), N-methylnicotinamide (9), N,N-dietylnicotinamide (10) (Sigma-Aldrich, Germany), isopropyl nicotinate (4), hexyl nicotinate (6) (Aldrich, Germany), benzyl nicotinate (7) (Fluka, Switzerland), 3-pyridinecarbaldehyde (11), 3-pyridinecarbonitrile (12), 3-pyridylmethanol (13), and methyl 3-pyridyl ketone (14) (E.Merck, Germany) were used as test solutes. The purities of the studied standard samples were at least 97%. Standard solutions of nicotinic acid and its derivatives (40 mg/10 mL) were prepared in ethanol (96%, pure for analysis, POCh, Gliwice, Poland).

Application of Reversed–Phase Thin–Layer Chromatography for Determination of Chromatographic Parameters of Lipophilicity

Reversed partition thin–layer chromatography (RP-TLC) was done on RP-2 plates (Kieselgel 60 F_{254} silanisiert, E. Merck, #1.05747). Solutions of the standards, 3-pyridinecarboaldehyde, 3-pyridinecarbonitrile, 3-pyridylmethanol, and methyl 3-pyridyl ketone, were spotted manually using a

microcapillary (Camag, Switzerland) onto the plates in 10 μL quantities, and the remaining compounds in 3 μL quantities. The chromatograms were developed by using the mixture of methanol + water ($pH_{water} = 2.53$; 5.88; 8.11); the content of methanol in mobile phase was gradually varied by 5% (%, v/v) from 40–100 (%, v/v).

Fifty mL of mobile phase was placed into a classical chromatographic chamber (Camag, Switzerland). The chamber was saturated with solvent for 30 min. The chromatograms were developed at the room temperature, e.g., 22(±1)°C. The development distance was 14 cm. The plates were dried at the room temperature, e.g., 22(±1)°C. After development and drying, the detection of substances on chromatogram was carried out using a densitometer (Camag TLC Scanner 3). On the basis of chromatograms obtained, the R_F values were calculated and converted to R_M values.

The R_M values obtained for studied nicotinic acid and its derivatives on Kieselgel 60 F_{254} silanized plates (RP-2), using the methanol + water ($pH_{water} = 2.53$; 5.88; 8.11) mobile phases were extrapolated to zero concentration of methanol in eluent (R_{MW}), in accordance with the Soczewiński-Wachtmeister equation:[14]

$$R_M = R_{MW} - S \cdot \varphi \tag{1}$$

where: R_M is the R_M value of examined substance by content φ of volume fraction of methanol in mobile phase; R_{MW} is the theoretical value of R_M of particular compound extrapolated to zero concentration of methanol in mobile phase; S is the slope of the regression curve; and, φ is the volume fraction of organic modifier in the mobile phase.

Calculation of Theoretical Partition Coefficients

The theoretical *n*-octanol-water partition coefficients, such as: AlogPs, IAlogP, ClogP, $logP_{Kowwin}$, xlogP, and miLogP were obtained from an internet data base.[15–18] The experimental partition coefficients for the compounds (with the exception of isopropyl nicotinate) were obtained from the same internet data base.[16]

RESULTS AND DISCUSSION

The lipophilicity of nicotinic acid and its derivatives were studied. The theoretical partition coefficients calculated by use of different methods and for experimental n-octanol-water partition coefficients for investigated compounds are presented in Table 1.

TABLE 1 The Numerical Values of Experimental and Theoretical *n*-Octanol-Water Partition Coefficients of Investigated Compounds[15–17]

	logP						
Compound No.	$logP_{exp}$	AlogPs	IAlogP	ClogP	$logP_{Kowwin}$	xlogP	miLogP
1	0.36	0.11	0.59	0.80	0.69	0.39	0.637
2	0.83	0.61	0.82	0.77	0.64	0.71	1.189
3	1.32	1.27	1.33	1.30	1.33	1.13	1.593
4	–	1.65	1.64	1.61	1.55	1.59	2.296
5	2.27	2.16	2.29	2.35	2.11	2.06	2.461
6	3.51	3.12	3.27	3.41	3.10	3.19	3.329
7	2.40	2.25	2.00	2.60	2.35	2.42	2.793
8	−0.37	−0.67	−0.16	−0.21	−0.45	−0.34	−0.326
9	0.00	−0.23	0.32	0.11	0.02	0.18	0.260
10	0.33	0.65	1.58	0.56	0.52	1.16	1.161
11	0.29	0.20	0.31	0.57	0.52	0.47	0.940
12	0.36	0.36	0.57	0.27	0.35	0.49	0.506
13	−0.02	−0.13	0.18	0.06	−0.11	–	0.443
14	0.43	0.45	0.65	0.48	0.49	0.61	0.869

Nicotinic acid and its derivatives were investigated with the use reversed-phase thin layer chromatography on Kieselgel 60 F_{254} silanized plates (RP-2), using methanol + water ($pH_{water} = 2.53; 5.88; 8.11$) in different volume compositions as a mobile phase. The R_M values obtained for studied compounds were extrapolated to a zero concentration of methanol in mobile phase in accordance with the Soczewiński-Wachtmeister Eq. (1). The terms of the regression equations (Eqs. (2–43)), describing the dependence of the R_M values of the nicotinic acid and its derivatives on the methanol content (φ) of the mobile phase are listed in Tables 2–4 for analysis performed on RP-2 plates ($R_M = R_{MW(pH=2.53)} - S_{(pH=2.53)} \cdot \varphi$; $R_M = R_{MW(pH=5.88)} - S_{(pH=5.88)} \cdot \varphi$; $R_M = R_{MW(pH=8.11)} - S_{(pH=8.11)} \cdot \varphi$), respectively.

Obtained by using the methanol + water ($pH_{water} = 2.53$) and methanol + water ($pH_{water} = 8.11$) mobile phase on RP-2 plates, the chromatographic parameters of lipophilicity R_{MW} indicated that hexyl nicotinate has the highest lipophilicity; whereas, nicotinic acid has the lowest lipophilicity.

Obtained by using the methanol + water ($pH_{water} = 5.88$) mobile phase on RP-2 plates, the chromatographic parameters of lipophilicity R_{MW} indicated that hexyl nicotinate has the highest lipophilicity; whereas, nicotinamide has the lowest lipophilicity.

It was found there was a relatively high correlation between the chromatographic parameters of lipophilicity R_{MW} and the slope of the regression curve S with Eq. (1) for compounds investigated on RP-2 plates using methanol + water ($pH_{water} = 2.53$; 5.88; 8.11) as the mobile phase. The regression equations (44)–(46) describe these linear relationships with

TABLE 2 Parameters of the Linear Regression (±SE) Relating the R_M Values of Nicotinic Acid and Its Derivatives to the Methanol Content (φ) of Methanol – Water ($pH_{water} = 2.53$) Mobile Phase (According to Eq. (1): $R_M = R_{MW(pH=2.53)} - S_{(pH=2.53)} \cdot \varphi$) for Analysis Performed on RP-2 Plates

Compound No.	$R_{MW(pH=2.53)}$ (±SE)	$S_{(pH=2.53)}$ (±SE)	n	r	SEE	F	Eq. No.
1	−0.184 (±0.156)	1.54 (±0.21)	5	0.972	0.052	51	(2)
2	0.868 (±0.077)	1.78 (±0.11)	10	0.984	0.054	250	(3)
3	1.237 (±0.068)	2.15 (±0.10)	10	0.992	0.047	479	(4)
4	1.588 (±0.061)	2.50 (±0.09)	10	0.995	0.043	788	(5)
5	2.052 (±0.055)	2.96 (±0.08)	10	0.997	0.039	1356	(6)
6	2.898 (±0.082)	3.80 (±0.12)	10	0.996	0.057	1022	(7)
7	2.271 (±0.088)	3.26 (±0.13)	10	0.994	0.062	643	(8)
8	−0.087 (±0.052)	0.97 (±0.08)	7	0.985	0.035	164	(9)
9	0.180 (±0.091)	1.22 (±0.13)	10	0.956	0.064	84	(10)
10	0.742 (±0.091)	1.71 (±0.13)	10	0.976	0.064	165	(11)
11	0.483 (±0.039)	1.57 (±0.06)	7	0.996	0.024	699	(12)
12	0.505 (±0.040)	1.53 (±0.06)	7	0.996	0.025	620	(13)
13	0.300 (±0.071)	1.37 (±0.10)	9	0.981	0.053	175	(14)
14	0.483 (±0.036)	1.40 (±0.05)	7	0.996	0.022	657	(15)

Where: SE – standard error; n – number of points to drive the particular regression equation; r – correlation coefficient; SEE – standard error of the estimation; F – the values of the Fisher test; for all regression equation the significance level (p) is $p < 0.01$.

high correlation coefficients:

$$R_{MW(pH=2.53)} = -1.196(\pm 0.146) + 1.083(\pm 0.068) \cdot S_{(pH=2.53)}$$
$$n = 14; \quad r = 0.9770; \quad SEE = 0.207; \quad F = 252; \quad p < 0.001 \tag{44}$$

TABLE 3 Parameters of the Linear Regression (±SE) Relating the R_M Values of Nicotinic Acid and Its Derivatives to the Methanol Content (φ) of Methanol – Water ($pH_{water} = 5.88$) Mobile Phase (According to Eq. (1): $R_M = R_{MW(pH=5.88)} - S_{(pH=5.88)} \cdot \phi$) for Analysis Performed on RP-2 Plates

Compound No.	$R_{MW(Ph=5.88)}$ (±SE)	$S_{(pH=5.88)}$ (±SE)	n	r	SEE	F	Eq. No.
1	0.489 (±0.154)	2.87 (±0.25)	4	0.992	0.037	132	(16)
2	0.810 (±0.108)	1.65 (±0.15)	12	0.963	0.091	127	(17)
3	1.132 (±0.108)	1.97 (±0.14)	12	0.974	0.091	183	(18)
4	1.453 (±0.096)	2.29 (±0.13)	12	0.984	0.081	313	(19)
5	1.920 (±0.105)	2.75 (±0.14)	12	0.987	0.088	378	(20)
6	2.706 (±0.097)	3.52 (±0.13)	12	0.993	0.081	732	(21)
7	2.127 (±0.113)	3.04 (±0.15)	12	0.988	0.095	396	(22)
8	0.116 (±0.089)	1.27 (±0.14)	8	0.966	0.055	85	(23)
9	0.352 (±0.059)	1.43 (±0.09)	10	0.986	0.042	272	(24)
10	0.671 (±0.072)	1.54 (±0.10)	12	0.981	0.061	250	(25)
11	0.358 (±0.065)	1.31 (±0.09)	12	0.979	0.054	227	(26)
12	0.357 (±0.066)	1.26 (±0.09)	12	0.976	0.055	204	(27)
13	0.170 (±0.061)	1.10 (±0.08)	12	0.973	0.051	178	(28)
14	0.385 (±0.076)	1.21 (±0.10)	12	0.966	0.064	140	(29)

Where: SE – standard error; n – number of points to drive the particular regression equation; r – correlation coefficient; SEE – standard error of the estimation; F – the values of the Fisher test; for all regression equation the significance level (p) is $p < 0.01$.

TABLE 4 Parameters of the Linear Regression (±SE) Relating the R_M Values of Nicotinic Acid and Its Derivatives to the Methanol Content (φ) of Methanol – Water ($pH_{water} = 8.11$) Mobile Phase (According to Eq. (1): $R_M = R_{MW(pH=8.11)} - S_{(pH=8.11)} \cdot \varphi$) for Analysis Performed on RP-2 Plates

Compound No.	$R_{MW(Ph=8.11)}$ (±SE)	$S_{(pH=8.11)}$ (±SE)	n	r	SEE	F	Eq. No.
1	−0.173 (±0.088)	1.53 (±0.15)	5	0.986	0.040	107	(30)
2	0.850 (±0.084)	1.63 (±0.11)	12	0.977	0.071	207	(31)
3	1.188 (±0.092)	1.96 (±0.12)	12	0.981	0.077	252	(32)
4	1.532 (±0.085)	2.33 (±0.11)	12	0.988	0.071	417	(33)
5	1.988 (±0.103)	2.79 (±0.14)	12	0.988	0.086	405	(34)
6	2.800 (±0.114)	3.60 (±0.15)	12	0.991	0.095	550	(35)
7	2.182 (±0.116)	3.06 (±0.16)	12	0.987	0.097	383	(36)
8	−0.120 (±0.045)	0.88 (±0.06)	6	0.990	0.019	200	(37)
9	0.153 (±0.067)	1.08 (±0.09)	7	0.982	0.041	139	(38)
10	0.869 (±0.086)	1.84 (±0.12)	11	0.981	0.066	232	(39)
11	0.578 (±0.089)	1.65 (±0.12)	11	0.976	0.068	178	(40)
12	0.639 (±0.105)	1.69 (±0.15)	11	0.967	0.081	132	(41)
13	0.596 (±0.084)	1.81 (±0.12)	6	0.990	0.039	208	(42)
14	0.645 (±0.077)	1.60 (±0.11)	9	0.984	0.059	218	(43)

Where: SE – standard error; n – number of points to drive the particular regression equation; r – correlation coefficient; SEE – standard error of the estimation; F – the values of the Fisher test; for all regression equation the significance level (p) is $p < 0.001$.

$$R_{MW(pH=5.88)} = -0.796(\pm 0.298) + 0.889(\pm 0.142) \cdot S_{(pH=5.88)}$$
$$n = 14; \quad r = 0.8743; \quad SEE = 0.413; \quad F = 39; \quad p < 0.01 \tag{45}$$

$$R_{MW(pH=8.11)} = -1.226(\pm 0.183) + 1.125(\pm 0.088) \cdot S_{(pH=8.11)}$$
$$n = 14; \quad r = 0.9656; \quad SEE = 0.236; \quad F = 165; \quad p < 0.001 \tag{46}$$

Equations (44), (45), and (46) confirm the fact that studied derivatives of nicotinic acid comply with the Soczewiński-Wachtmeister Eq. (1). This result proves that the nicotinic acid derivatives can be regarded as compounds belonging to the same group under the conditions described.

It was stated that the lipophilicity R_{MW} values correlate well with the experimental partition coefficients ($logP_{exp}$) for the compounds investigated (Figures 1–3). Obtained by using the methanol + water ($pH_{water} = 2.53$) and methanol + water ($pH_{water} = 8.11$) mobile phase on RP-2 plates, the chromatographic parameters of lipophilicity R_{MW} of nicotinic acid are far from the regression line (Figures 1 & 3). Nicotinic acid has the lowest lipophilicity under the chromatographic conditions used. However, experimental partition coefficients ($logP_{exp}$) indicated that, from among all compounds examined, nicotinamide has the lowest lipophilicity. Therefore, it can be supposed that nicotinic acid dissociates are applied in these chromatographic conditions.

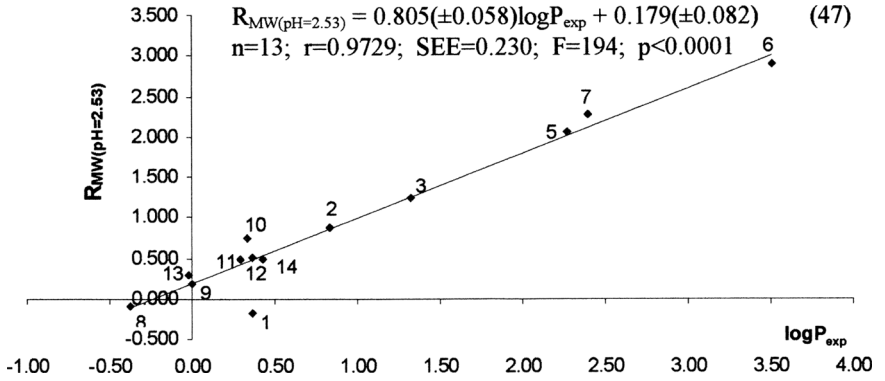

FIGURE 1 Relationship between the chromatographic parameter of lipophilicity R_{MW} obtained on RP-2 plates using methanol + water ($pH_{water} = 2.53$) mobile phase and experimental partition coefficients ($logP_{exp}$) for the compounds investigated.

The best stated agreement was with the experimental partition coefficients ($logP_{exp}$) and the chromatographic parameter of lipophilicity R_{MW} for compounds investigated on RP-2 plates and by use of the methanol + water ($pH_{water} = 5.88$) mobile phase (Figure 2).

The values of correlation coefficients of linear relationships between the chromatographic parameters of lipophilicity and experimental, as well as theoretical partition coefficients for all studied compounds, are presented in Table 5 and indicate that:

- Obtained by using methanol + water ($pH_{water} = 2.53$) mobile phase on the RP-2 plates, the chromatographic parameter of lipophilicity R_{MW}

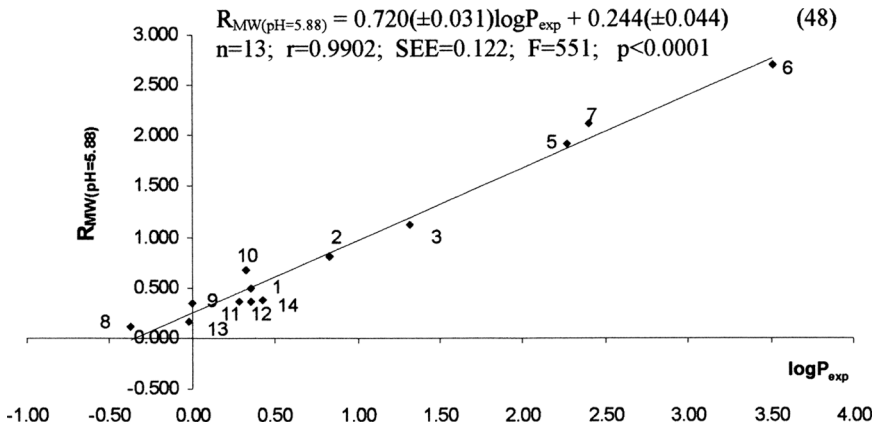

FIGURE 2 Relationship between the chromatographic parameter of lipophilicity R_{MW} obtained on RP-2 plates using methanol + water ($pH_{water} = 5.88$) mobile phase and experimental partition coefficients ($logP_{exp}$) for the compounds investigated.

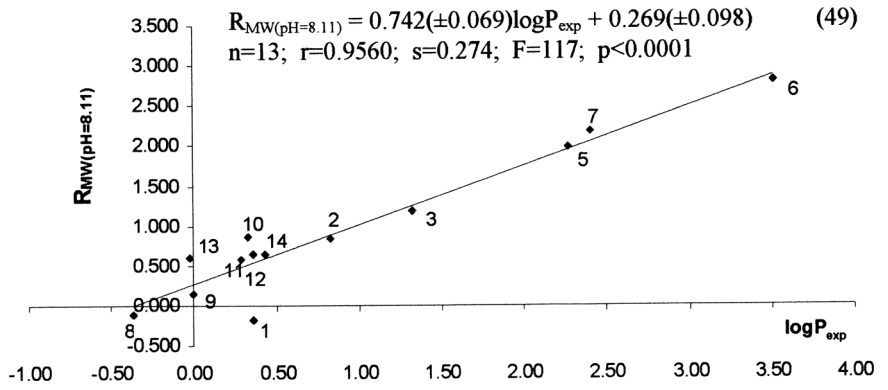

FIGURE 3 Relationship between the chromatographic parameter of lipophilicity R_{MW} obtained on RP-2 plates using methanol + water ($pH_{water} = 8.11$) mobile phase and experimental partition coefficients ($logP_{exp}$) for the compounds investigated.

correlated best with the theoretical partition coefficient AlogPs:

$$R_{MW(pH=2.53)} = 0.248(\pm0.065) + 0.836(\pm0.048) \cdot \text{AlogPs}$$
$$n = 14; \quad r = 0.9805; \quad SEE = 0.191; \quad F = 299; \quad p < 0.0001 \tag{50}$$

- Obtained by using methanol + water ($pH_{water} = 5.88$) mobile phase on the RP-2 plates, the chromatographic parameter of lipophilicity R_{MW} correlated best with the theoretical partition coefficients ClogP, $logP_{Kowwin}$ and AlogPs:

$$R_{MW(pH=5.88)} = 0.144(\pm0.048) + 0.752(\pm0.032) \cdot \text{ClogP}$$
$$n = 14; \quad r = 0.9891; \quad SEE = 0.125; \quad F = 540; \quad p < 0.0001 \tag{51}$$
$$R_{MW(pH=5.88)} = 0.194(\pm0.060) + 0.788(\pm0.044) \cdot logP_{Kowwin}$$
$$n = 14; \quad r = 0.9814; \quad SEE = 0.163; \quad F = 314; \quad p < 0.0001 \tag{52}$$
$$R_{MW(pH=5.88)} = 0.314(\pm0.058) + 0.732(\pm0.043) \cdot \text{AlogPs}$$
$$n = 14; \quad r = 0.9803; \quad SEE = 0.168; \quad F = 295; \quad p < 0.0001 \tag{53}$$

- Obtained by using methanol + water ($pH_{water} = 8.11$) mobile phase on the RP-2 plates, the chromatographic parameter of lipophilicity R_{MW} correlated best with the theoretical partition coefficients xlogP and AlogPs:

$$R_{MW(pH=8.11)} = 0.055(\pm0.089) + 0.883(\pm0.062) \cdot \text{xlogP}$$
$$n = 13; \quad r = 0.9741; \quad SEE = 0.213; \quad F = 204; \quad p < 0.0001 \tag{54}$$

TABLE 5 The Values of Correlation Coefficients of Linear Relationships Between Theoretical and Experimental Partition Coefficients as well as Chromatographic Parameters of Lipophilicity

	$R_{MW(pH=2.53)}$	$R_{MW(pH=5.88)}$	$R_{MW(pH=8.11)}$	$logP_{exp}$	AlogPs	IAlogP	ClogP	$logP_{Kowwin}$	xlogP	miLogP
$R_{MW(pH=2.53)}$	1									
$R_{MW(pH=5.88)}$	0.9737	1								
$R_{MW(pH=8.11)}$	0.9939	0.9513	1							
$logP_{exp}$	**0.9729**	**0.9902**	**0.9560**	1						
AlogPs	**0.9805**	**0.9803**	**0.9726**	0.9882	1					
IAlogP	0.9410	0.9551	0.9336	0.9460	0.9689	1				
ClogP	0.9532	**0.9891**	0.9341	0.9910	0.9782	0.9437	1			
$logP_{Kowwin}$	0.9523	**0.9814**	0.9352	0.9892	0.9862	0.9481	0.9952	1		
xlogP	0.9724	0.9764	**0.9741**	0.9719	0.9877	0.9792	0.9724	0.9761	1	
miLogP	0.9699	0.9694	0.9627	0.9761	0.9880	0.9492	0.9717	0.9788	0.9799	1

$$R_{MW(pH=8.11)} = 0.326(\pm 0.072) + 0.776(\pm 0.053) \cdot \text{AlogPs}$$
$$n = 14; \quad r = 0.9726; \quad SEE = 0.211; \quad F = 210; \quad p < 0.0001 \tag{55}$$

It was also stated that ClogP correlates best with experimental partition coefficients $\log P_{exp}$ of the compounds studied:

$$\log P_{exp} = -0.14(\pm 0.06) + 1.03(\pm 0.04) \cdot \text{ClogP}$$
$$n = 13; \quad r = 0.9910; \quad SEE = 0.16; \quad F = 604; \quad p < 0.0001 \tag{56}$$

CONCLUSIONS

The best stated agreement was with the experimental partition coefficients ($\log P_{exp}$) and the chromatographic parameter of lipophilicity R_{MW} for compounds investigated on the RP-2 plates and by use of a methanol + water ($pH_{water} = 5.88$) mobile phase. Hexyl nicotinate has the highest lipophilicity and nicotinamide the lowest, under the chromatographic conditions used.

The chromatographic parameters of lipophilicity and theoretical n-octanol-water partition coefficients may be the alternative methods of lipophilicity determination of examined nicotinic acid and its derivatives.

The methods of determining lipophilicity on the basis of a theoretical calculation of log P and chromatographic methods complement other well-established methods and applications, that is, methods of normal measurement with the *n*-octanol–water system. Due to experimental difficulties (e.g., solubility limits, chemical instability, formation of emulsions, impure compounds), evaluation of log P values by the analytical methods described in this paper is justified. The methodology described in this paper can be used for study and comparison of the lipophilic properties of other organic compounds of biological significance.

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REFERENCES

1. Pyka, A. Selected Bile Acids, Analysis by TLC. In *Encyclopedia of Chromatography*, 3rd Ed.; Cazes, J., Ed.; Taylor and Francis: 2010, pp 1–11.

2. Pyka, A. Topological Indices: TLC. In *Encyclopedia of Chromatography*, 3rd Ed.; Cazes, J., Ed.; Taylor and Francis: 2010, pp 1–11.
3. Pyka, A.; Dołowy, M. Lipophilicity of Selected Bile Acids as Determined by TLC. I. *J. Liq. Chromatogr.* 2003, 26 (16), 2741–2750.
4. Pyka, A.; Dołowy, M. Lipophilicity of Selected Bile Acids as Determined by TLC. II. Investigations on RP18 W Stationary Phase. *J. Liq. Chromatogr.* 2005, 28, 297–311.
5. Pyka, A.; Dołowy, M. Lipophilicity of Selected Bile Acids as Determined by TLC. III. Investigations on RP2 Stationary Phase. *J. Liq. Chromatogr.* 2005, 28, 1765–1775.
6. Pyka, A.; Dołowy, M.; Gurak, D. Lipophilicity of Selected Bile Acids, as Determined by TLC. IV. Investigations on CNF_{254} Stationary Phase. *J. Liq. Chromatogr.* 2005, 28, 2705–2717.
7. Pyka, A.; Babuśka, M. Lipophilicity of Selected Steroid Compounds. I. Investigations on RP18 W Stationary Phase by RP-HPTLC. *J. Liq. Chromatogr.* 2006, 29, 1891–1903.
8. Mrkvičková, Z.; Kovařiková, P.; Klimeš, J.; Doležal, M. Determination of the Lipophilicity of Potential Antituberculotic Compounds by RP-TLC. *J. Planar Chromatogr.- Mod. TLC* 2006, 19, 422–426.
9. Flieger, J.; Tatarczak, M.; Wujec, M.; Pitucha, M.; Szumiło, H. RP-TLC Determination of Lipophilicity of Some New Derivatives of 1,2,4-triazole and Thiosemicarbazide with Potential Antituberculosis Activity. *J. Planar Chromatogr.- Mod. TLC* 2006, 19, 32–41.
10. Perišić-Janjić, N.; Gyöngyi, V.; Tomić, J.; Petrović, S. Effect of the Physicochemical Properties of *N,N*-disubstituted-2-phenylacetamide Derivatives on their Retention Behavior in RP-TLC. *J. Planar Chromatogr.- Mod. TLC* 2007, 20 (5), 353–359.
11. Gumieniczek, A.; Berecka, A.; Matosiuk, D.; Hopkała, H. Standarized Reversed-Phase Thin-Layer Chromatographic Study of the Lipophilicity of Five Anti-Diabetic Thiazolidinediones. *J. Planar Chromatogr.- Mod. TLC* 2007, 20 (4), 261–265.
12. Pyka, A. Study of Lipophilicity and Application of Selected Topological Indexes in QSAR Analysis of Nicotinic Acid Derivatives. Part I. *J. Planar Chromatogr.- Mod. TLC* 2004, 17, 275–279.
13. Pyka, A.; Klimczok, W. Study of Lipophilicity and Application of Selected Structural Descriptors in QSAR Analysis of Nicotinic Acid Derivatives. Investigations on RP18WF254 Plates. Part II. *J. Planar Chromatogr.- Mod. TLC* 2005, 18, 300–304.
14. Jóźwiak, K.; Szumiło, H.; Soczewiński, E. Lipophilicity, Methods of Determination and Its Role in Biological Effect of Chemical Substances. *Wiad. Chem.* 2001, 55, 1047–1074. (in Polish)
15. Interactive Analysis logP Predictors. www.logp.com (accessed September 28, 2003).
16. Tetko, I. V.; Tanchuk, V. Yu. Virtual Computational Chemistry Laboratory, VCC-lab. 2002. http://146.107.217.178/servlets/vcclab?action=alogps (accessed September 28, 2003).
17. miLogP1.2, Molinspiration Property Calculation Service FAQ, http://www.molinspiration.com (accessed September 28, 2003).
18. Mannhold, R.; Dross, K. Calculation Procedures for Molecular Lipohilicity: A Comparative Study. *Quant. Struct. Act. Relat.* 1996, 15, 403–409.