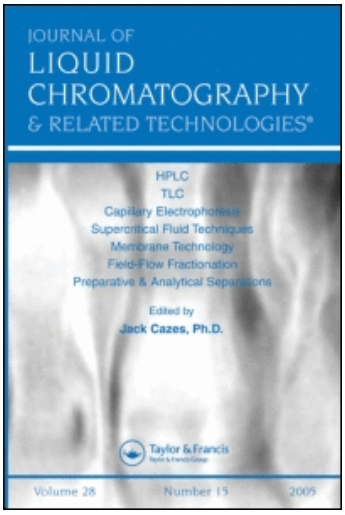

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Prediction of the Lipophilicity of Some Plant Growth Stimulators by RP-TLC and Relationship Between Slope and Intercept of TLC Equations

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Prediction of the Lipophilicity of Some Plant Growth Stimulators by RP-TLC and Relationship Between Slope and Intercept of TLC Equations

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Abstract: Using RP-TLC with RP-18 F_{254s} and a methanol-water mixture as the mobile phase, several new compounds (some plant growth stimulators, such as amido esters of ethanolamine and maleic and succinic acid derivatives) were studied. The log *P* values were calculated using fragmental constant or ACD/Labs Software database (Toronto, Canada). A good correlation was obtained between log *P* vs. R_{M0} and C_0, respectively. These relationships can be used for prediction of the lipophilicity of similar compounds from the same structural group. The relationship between intercepts and slopes from TLC equations showed a very good correlation. The results obtained by RP-TLC demonstrated a basic feature of lipophilicity; that both series of compounds are two "congeneric" series.

Keywords: Plant growth stimulators, RP-TLC, TLC equations, Lipophilicity, Log *P* vs. R_{M0} and C_0, Intercept vs slope

INTRODUCTION

Lipophilicity can be determined by the traditional partition method between *n*-octanol and water using shake flask experiments.[1] The octanol-water

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system is used in most partition studies but the determination of the partition coefficient, P, by equilibration methods is difficult. The difficulties can be overcome as proposed by Boyce and Milborrow[2] using chromatographic methods. Bate-Smith and Westfal[3] introduced the term, $R_M = \log [(1/R_F) - 1]$, which leads to a linear correlation between the partition coefficient, log P, and R_M values (R_F being the ratio between the distance migrated by the compound and the distance migrated by the solvent front). The RP-TLC equation for one compound is represented by a linear relationship between the R_M values and the organic solvent concentrations in the mobile phase. The correlations between log P, and extrapolated (at zero percent organic solvent) values for k' or R_{M0}, are frequently linear for homologues series in a reversed-phase liquid chromatography (RP-LC). Many studies[4–9] have shown that the lipophilicity, as well as the specific hydrophobic surface of a solute can be determined from the linear relationship between the R_{M0} values and the concentration of methanol in the mobile phase.

In order to understand the relationship between slopes and intercepts of the linear TLC equations, the physicochemical meaning of this parameter has to be discussed. The intercept R_{M0} can be considered as a measure of the partitioning of the component between a non-polar stationary phase and a polar mobile phase in RP-TLC.

The slope can be interpreted from different points of view:[10] as reflecting the nature of the compound; in this case is mainly determined by the interaction between the solute and eluent; -in terms of the *displacement model*, as the number of eluent molecules present in the solvation sphere of the solute,[11] or on the basic concept of *hydrophobic surface area availability*.[12]

As a consequence, the slope of this surface might be the critical factor for differentiating a series of *congeneric compounds.* Many experimental data[13,14] show that the correlation between the intercept, R_{M0}, and the slope of the linear TLC equation is maintained only within a series of *congeneric compounds*. The congenerity can be broken down by the presence of ionizable groups, which can modify the interactions of compounds under experimental TLC conditions,[10] and the factors that affect chromatographic congenerity.[15]

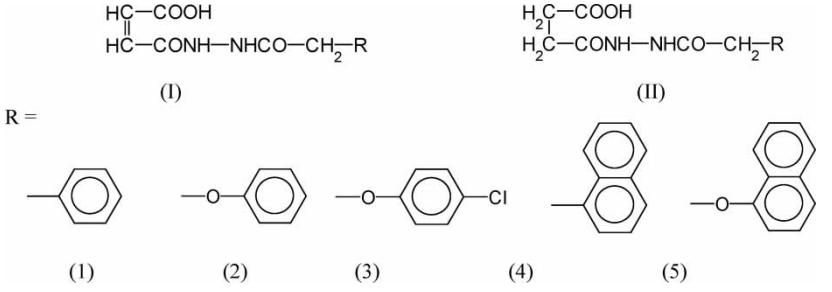
A recent study used the parameter C_0 (where $C_0 = R_{M0}/slope$) instead of R_{M0}. vs. log P. However, the correlations between the lipophilicity term, C_0, and log P were not better than R_{M0}. vs. log P, in all the studied cases.[16–18]

The purpose of this paper is to review the main aspects of our chromatographic data and reexamine the entire relationship log $P =$ f (R_{M0}), evaluating if the relationship between R_{M0} and the slope is an essential feature only for *congeneric compounds*.[10,19–22]

EXPERIMENTAL

The RP-TLC technique was performed on 10 × 10 mm HP-TLC plates coated with silica gel RP-18 F_{254S} and were obtained from Merck (Darmstadt,

Table 1. The structures of the maleic and succinic acid derivatives



Compound	1	2	3	4	5	6	7	8	9	10
	I.1	I.2	I.3	I.4	I.5	II.1	II.2	II.3	II.4	II.5

Germany). Methanol of chromatography grade was obtained from Reactivul (Bucharest, Romania). The plates were developed in an ascending mode in a saturated eluent in a vertical nano chamber [10 × 10 cm from Desaga (Wiesloch, Germany)]. The saturation of the chamber was performed by lining of the chromatographic chamber with filter paper. The migration distances of the eluent between start and front was 8 cm in all instances. The spots were detected under UV light at 254 nm (Camag universal UV lamp). The R_M values were plotted *versus* methanol molar fraction in water, and a linear correlation was obtained.[23,24] The structures of the studied compounds are shown in Tables 1 and 2.

RESULTS AND DISCUSION

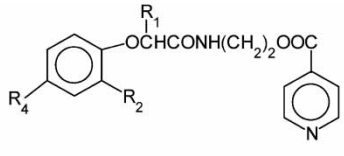
In a previous paper[23] we presented experimental data concerning TLC equations for maleic and succinic acid derivatives only ($R_M = a_0 + a_1 X$), where X is the molar fraction of the organic solvent in mobile phase; we will now present other correlations between Log P as a function of R_{M0} and C_0, respectively.

The log P values of maleic, succinic, and phthalic acid derivatives from Table 1 were calculated using ACD/Labs Software (Toronto, Canada).[25] The relationship between the calculated log P values and the extrapolated R_{M0} and C_0 values are given by Equations (1) and (2), and Figure 1.

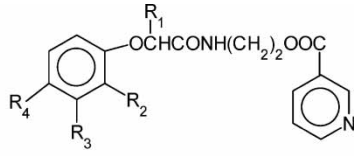
$$\begin{aligned} \text{Log}\, P = & 1.8895\ (\pm 0.2139)\ R_{M0} + 0.4558\ (\pm 0.1184) \\ & \text{n} = 10,\ \text{r} = 0.9813 \end{aligned} \tag{1}$$

where n is the number of studied compounds and r is the correlation coefficient.

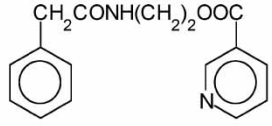
Table 2. The structures of the amido esters of ethanolamine



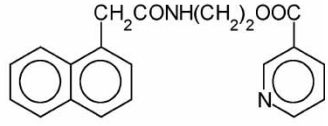
Compound 1-6



Compound 7-12



Compound 13



Compound 14

Compound	R_1	R_2	R_3	R_4
1	H	H		H
2	H	H		Cl
3	C_2H_5	H		H
4	CH_3	H		H
5	H	CH_3		H
6	H	Cl		Cl
7	C_2H_5	H	H	H
8	CH_3	H	H	H
9	H	H	CH_3	H
10	H	CH_3	H	H
11	H	Cl	H	Cl
12	H	H	H	Cl

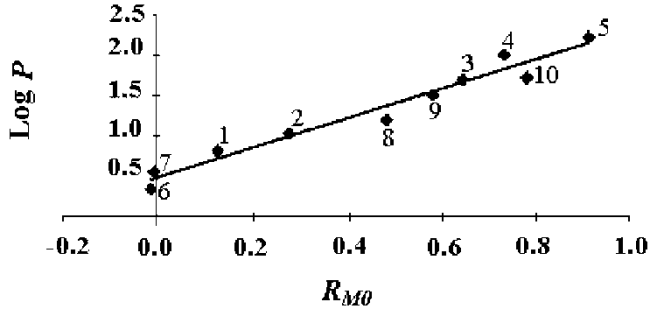


Figure 1. Relationship between log P and R_{M0} for the maleic and succinic acid derivatives.

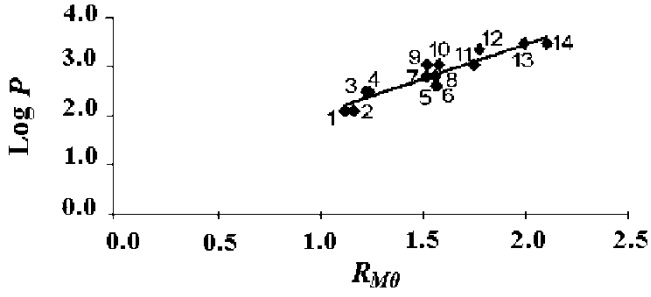


Figure 2. Relationship between log P and R_{M0} for the amido esters of ethanolamine.

$$\text{Log}\,P = -3.2148\ (\pm 0.5643)\ C_0 + 0.4028\ (\pm 0.1897)$$
$$\text{n} = 10,\ \text{r} = 0.9568 \tag{2}$$

The chromatographic experiments[24] showed a good correlation between the R_{M0} and C_0 values vs. log P, for amido esters of ethanolamine as shown in Table 2 and Figure 2.

$$\text{Log}\,P = 0,5871\ (\pm 0.5246)\ R_{M0} + 1.4310\ (\pm 0.3314)$$
$$\text{n} = 14,\ \text{r} = 0.9281 \tag{3}$$

$$\text{Log}\,P = -8.2883\ (\pm)\ C_0 - 2.2258\ (\pm 0.3314)$$
$$\text{n} = 14,\ \text{r} = 0.8902 \tag{4}$$

The present study uses data from our previously published work,[23,24] trying to asses whether the relationship between R_{M0} and slope (a_1) can be considered a basic feature of the RP-TLC determination of lipophilicity. The equations describing the correlations between R_{M0} and the slope for

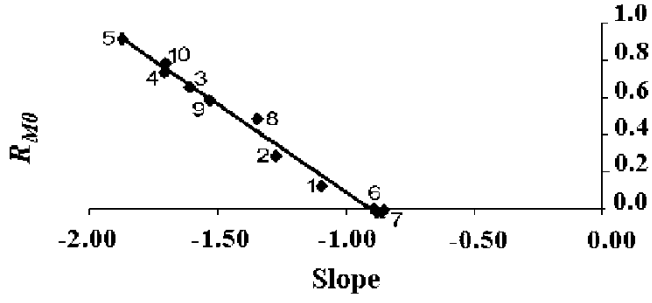


Figure 3. Relationship between R_{M0} and slope for the maleic and succinic acid derivatives.

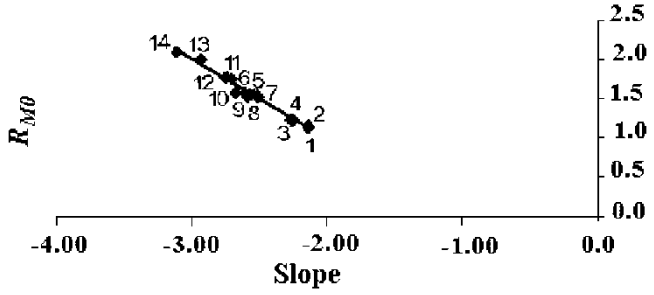


Figure 4. Relationship between R_{M0} and slope for the amido esters of ethanolamine.

two different series of compounds from Table 1 and 2 are given by Equations (5) and (6), which are shown in Figures 3 and 4.

$$R_{M0} = -0.9396\ (\pm 0.0660)\ \text{slope} - 0.8502\ (\pm 0.0940)$$
$$\text{n} = 10, \text{r} = 0.9927 \tag{5}$$

$$R_{M0} = -1.0228(\pm 0.0846)\,\text{slope} - 1.0407(\pm 0.2162)$$
$$\text{n} = 14, \text{r} = 0.9899 \tag{6}$$

The correlations for log P vs. C_0 are no better than log P vs. R_{M0} as is demonstrated by Equations (1)–(4). On the other hand, the high values of the correlation constant, r, show that R_{M0} can be considered a measure of the compound's lipophilicity. Thus, as the R substituent increases in size and hydrophobicity, a simultaneous increase in R_{M0} is observed for the maleic and succinic acid derivatives.

The "congenerity" of compounds can be expressed in RP-TLC by the linearity between the extrapolated parameters R_{M0} and the slope (Equations (5)–(6). The results obtained by RP-TLC demonstrated that both groups can be considered as two "congeneric" series. The relationship between slope and intercept of the TLC equations can be interpreted as an important aspect of the chromatographic determination of lipophilicity for strictly congeneric compounds.

CONCLUSIONS

RP-HPTLC is a powerful method for determination of the lipophilicity of "congeneric" compounds. The results obtained by RP-TLC showed a good linear correlation between log P vs. R_{M0} or C_0. at the same time the correlation between R_{M0} vs. slope shows that maleic acid derivatives and amido esters of ethanolamine compounds constitute two "congeneric" series. These

relationships can be used to predict the lipophilicity of similar compound from the same structural group.

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