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Chromatographic Determination of Solubility of Low Soluble Substances The Physico-chemical Basis

Short Communication

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The physico-chemical basis for a direct chromatographic determination of solubility of low soluble substances by means of adsorption and partition TLC is discussed. This method is a practical consequence of the chromatographic "binary solutions" model, a new semi-empirical approach based on phenomenological thermodynamics.

(Keywords: Chromatography; Binary solutions model; Solubility; Thermodynamics)

Chromatographische Bestimmung der Löslichkeit von schwerlöslichen Substanzen. Die physikalisch-chemische Basis (Kurze Mitteilung)

Die physikalisch-chemische Basis einer direkten chromatographischen Bestimmung der Löslichkeit von schwerlöslichen Substanzen mit Hilfe der Adsorptions- und Verteilungsdünnschichtchromatographie wird diskutiert. Die Möglichkeit einer solchen Bestimmung ist die praktische Konsequenz des chromatographischen Modells der „binären Lösungen", einer neuen semi-empirischen, auf der phänomenologischen Thermodynamik begründeten Methode.

In papers [1-4] we introduced a new semi-empirical model of adsorption and partition chromatography based on thermodynamical premises. This model approximates each chromatographic system to the regular binary solution, composed of solvent and solute. Thus we defined the chromatographed substance as "solute", and the applied stationary phase as "solvent". Further we utilized the fundamental thermodynamic relationship, usually applied to regular solutions:

$$\Delta \mu_i = \mu_i - \mu_i^0 = RT \ln \frac{c_i}{c_i + c_{ch}} \cdot f_i, \tag{1}$$

where μ_i is the chemical potential of an i-th "solute" in the chromatographic "binary solution"; μ_i^0 is the chemical potential of an i-th substance in a hypothetical reference state; c_i and c_{ch} are molar concentrations of an i-th substance and stationary phase, respectively; f_i is the activity coefficient of the "solute".

The effective meaning of $\Delta \mu_i$ in TLC can be given by the following relationship:

$$\Delta \mu_i = \Delta \mu_{\mathrm{dissolv}} + \frac{n_s}{n_s + n_m} \cdot \Delta \mu_{\mathrm{part}}, \tag{2}$$

where $\Delta \mu_{\mathrm{dissolv}}$ is the change of the chemical potential, accompanying the transfer of one mole of an i-th substance from the quasi-pure form to the mobile phase; $\Delta \mu_{\mathrm{part}}$ is the change of the chemical potential accompanying the transfer of one mole of an i-th substance from the mobile to the stationary phase; n_s and n_m are molar amounts of an i-th substance in the stationary and the mobile phase, respectively.

$\Delta \mu_i$ can be calculated from eq. (1); in the case of the partition TLC $\Delta \mu_{\mathrm{part}}$ can be deduced from the *Martin-Synge* model [5, 6], while in the case of the adsorption TLC from the *Snyder* model [7, 8]. Thus eq. (2) allows determination of $\Delta \mu_{\mathrm{dissolv}}$, and consequently of the solubility of the chromatographed substance.

A) Partition TLC

The principal thermodynamic equation of the partition TLC is given below:

$$R'_f = \frac{1}{1 + K(V_s/V_m)}, \tag{3}$$

where R'_f is the thermodynamic R_f coefficient, K is partition constant, and V_s and V_m are volumes of stationary and mobile phase, respectively. From eq. (3) we can easily extract the K value. Thus $\Delta \mu_{\mathrm{part}}$ can be given by the following dependence:

$$\Delta \mu_{\mathrm{part}} = RT \ln K = RT \ln \frac{1 - R'_f}{R'_f} \cdot \frac{V_m}{V_s}. \tag{4}$$

K can also be defined as follows:

$$K = \frac{n_s}{n_m} \cdot \frac{V_m}{V_s}. \tag{5}$$

Thus combining eqs. (3) and (5) we can derive the following relationship:

$$\frac{n_s}{n_s + n_m} = 1 - R'_f. \tag{6}$$

Substituting eqs. (1), (4), and (6) to eq. (2) we obtain:

$$\begin{aligned}\Delta \mu_{\text{dissolv}} = RT \ln d_i \gamma_i = RT \ln \frac{c_i}{c_i + c_{ch}} \cdot f_i - \\ - (1 - R'_f)\, RT \ln \frac{1 - R'_f}{R'_f} \cdot \frac{V_m}{V_s},\end{aligned} \tag{7}$$

where d_i is the molar fraction of an i-th substance in a given solution, and γ_i is the respective activity coefficient. Transforming eq. (7) we get:

$$d_i \gamma_i = \frac{c_i f_i (R'_f V_s)^{1 - R'_f}}{(c_i + c_{ch})\, [(1 - R'_f)\, V_m]^{1 - R'_f}}. \tag{7a}$$

In the case of low soluble substances we can assume γ_i as equal to 1, and consequently we obtain the following and slightly simplified relationship:

$$d_i \simeq \frac{c_i f_i (R'_f V_s)^{1 - R'_f}}{(c_i + c_{ch})\, [(1 - R'_f)\, V_m]^{1 - R'_f}}. \tag{7b}$$

It is an established fact [9] that in the majority of cases the dynamic and static partition of a substance between two inmiscible phases are quantitatively similar. For this reason one can expect that eq. (7 b) can be employed for a reliable and simple direct estimation of solubility with low soluble substances.

B) Adsorption TLC

An analogous approach can be applied to adsorption TLC. The equation analogous to the *Martin-Synge* relationship was derived by *Snyder* (unsimplified version) and is given below:

$$R'_f = \frac{1}{1 + K_{th} [V_a W_a / (V_m - V_a W_a)]}, \tag{8}$$

where K_{th} is the thermodynamic partition constant, V_a is the volume of the adsorbed (i.e. immobilized) mobile phase per one gram of sorbent, and W_a is the weight of sorbent.

From eq. (8) we can easily extract K_{th}. Thus $\Delta \mu_{\text{part}}$ is given by the following relationship:

$$\Delta \mu_{\text{part}} = RT \ln K_{th} = RT \ln \frac{1 - R'_f}{R'_f} \cdot \frac{V_m - V_a W_a}{V_a W_a}. \tag{9}$$

K_{th} can also be defined as follows:

$$K_{th} = \frac{n_s}{n_m} \cdot \frac{V_m - V_a W_a}{V_a W_a}. \tag{10}$$

Combining eqs. (8) and (10) we obtain the same dependence as given by eq. (6). Substituting eqs. (1), (6), and (9) to eq. (2) we obtain the following relationship:

$$\begin{aligned} \Delta \mu_{\text{dissolv}} = RT \ln d_i \gamma_i = RT \ln \frac{c_i}{c_i + c_{ch}} \cdot f_i - \\ - (1 - R'_f)\, RT \ln \frac{1 - R'_f}{R'_f} \cdot \frac{V_m - V_a W_a}{V_a W_a}. \end{aligned} \tag{11}$$

Consequently:

$$d_i \gamma_i = \frac{c_i f_i (R'_f V_a W_a)^{1-R'_f}}{(c_i + c_{ch}) \left[(1 - R'_f)(V_m - V_a W_a)\right]^{1-R'_f}}; \tag{11 a}$$

$$d_i \simeq \frac{c_i f_i (R'_f V_a W_a)^{1-R'_f}}{(c_i + c_{ch}) \left[(1 - R'_f)(V_m - V_a W_a)\right]^{1-R'_f}}. \tag{11 b}$$

Thus, adsorption TLC can also be utilized to estimate the solubility of low soluble substances. Such direct and physico-chemically reasonable approach is a novelty in chromatography which is usually employed only in a practical and comparative way.

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