ON THE SOLUBILITY OF PESTICIDES AND COMPOUNDS OF PESTICIDE TYPE

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Introduction

The basic, and often one of the most difficult, problems of the preparation of formulations based on the suitable solubility of the active substance, thus e.g. of solutions, emulsifiable concentrates, etc., is the selection of a non-phytotoxic organic solvent or solvent combination, providing primarily for economic concentration. Even today, time and again lengthy experimental work is needed to establish the suitable solvent or solvent combination, and to decide whether a solution of adequate concentration can be prepared at all from the given active substance.

In view of the almost unlimited number of possible solvents, experimental work for solving the task may be rather time consuming, though the shortening of the time of experimental work needed for selection and decision is of primary interest.

The aim of the present work was the development of approximative methods for the solution of problems in conjunction with the solubility of solid pesticides, compounds of pesticide type and intermediates. Our work was based on the non irrealistic assumption that the measure of the expectable solubility of predominantly weakly polar pesticides of non-electrolytic character can be evaluated by using the so-called solubility parameters, based on the results of HILDEBRAND and SCOTT [1]. In the following, we report on the results of this study.

Theoretical part

Dissolution is known to proceed when the process is accompanied by a decrease in the free energy F of the system, i.e. for

$$\Delta F < 0, \tag{1}$$

where ΔF is the change in free energy of the system.

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In consideration of the fact that according to the second law of thermodynamics,

$$\Delta F = \Delta H - T\Delta S \tag{2}$$

where ΔH is the change in internal energy of the system (heat of dissolution),
ΔS is the change in entropy of the system,
T is the temperature of dissolution in K, the condition for the fulfillment of (1) will be the inequality

$$\Delta H < T \cdot \Delta S. \tag{3}$$

Since dissolution is always accompanied by an increase in entropy, according to (2) and (3) the value ΔH plays the most important role in dissolution.

According to HILDEBRAND [1], the energy of interaction of two different non-polar molecules is equal to the geometric mean value of the respective values of identical molecules. It follows that in the case of apolar and weakly polar substances the value of ΔH can be expressed by the characteristics of the solvent and of the substances to be dissolved or mixed according to:

$$\Delta H = \left[\left(\frac{\Delta E_1}{V_1}\right)^{\frac{1}{2}} - \left(\frac{\Delta E_2}{V_2}\right)^{\frac{1}{2}}\right]^2 \cdot \varphi_1 \cdot \varphi_2 \tag{4}$$

E_1 and E_2 are the internal heat of evaporation of the single components in Kcal,
V_1 and V_2 are the molar volumes of the components,
φ_1 and φ_2 are the molar fractions of the components.

The expression $\Delta E/V$ is the density of cohesion energy, that is to say, the energy needed for the separation of the molecules of pure substance contained in 1 ml, for overcoming the energy of interaction between the molecules. The square root of cohesion energy density is mentioned in the literature after HILDEBRAND as solubility parameter ϑ [1, 2, 3, 4]. When using the solubility parameter, Eq. (4) can be written in the following form:

$$H = V_{\ddot{o}}[\vartheta_1 - \vartheta_2]^2 \cdot \varphi_1 \cdot \varphi_2 \tag{5}$$

where $V_{\ddot{o}}$ is the total volume of the system in ml.

It follows from relationship (5) that dissolution is to be expected (ΔH is the smallest), when the difference between the solubility parameters of the solvent and of the substance to be dissolved is small. In the contrary case the value of ΔH exceeds that of $T\Delta S$, so that no dissolution takes place. According to experiences [5, 6, 7] the difference between ϑ_1 and ϑ_2 cannot be more than 1 to 1.5 $\left[\frac{\text{cal}}{\text{ml}}\right]^{\frac{1}{2}}$. The solubility parameter of solvent mixtures is formed additively in the ratio of the molar fractions of the components of the mixture, i.e.

$$\vartheta_{\text{mixture}} = n_1 \cdot \vartheta_1 + n_2 \cdot \vartheta_2 \tag{6}$$

where n_1 and n_2 are molar fractions,

ϑ_1 and ϑ_2 solubility parameters of the components forming the mixture.

Relationship (6) offers also the possibility to form a solvent mixture of adequate solution power by the admixture in suitable ratio of solvents, which each separately are not able to dissolve the solid substance.

The solubility parameters of several solvents are known from the literature [1, 2, 4]. The solubility parameter changes with temperature. The temperature dependence of ϑ is approximately described by [1]

$$\vartheta = \vartheta_0^{1.25 \cdot \alpha [T_0 - T]} \tag{7}$$

where ϑ is the solubility parameter at temperature T, K.

ϑ_0 is the solubility parameter at temperature T_0, K;

α is the thermal expansion coefficient.

It follows from Eq. (5) that the solubility of a solid of non-electrolyte character will be the highest in a solvent with a solubility parameter ϑ_1 equal to that of the solid substance ϑ_s. This implicates on the other hand that for the evaluation of the expected solubility of the solid substance, for the selection of the best solvent, the solubility parameter of the solid substance must also be known.

However, while the solubility parameters of many liquids have been published in the literature, or they can be calculated with good approximation by relatively simple methods from data easy to determine, the determination of the solubility parameters of solid substances is rather time consuming and cumbersome.

According to HILDEBRAND [1], the solubility parameters of solid substances can be determined from solubility data, when solvents of known solubility parameters are used:

$$\lg \frac{x_s^i}{x_s} = \frac{V_S \cdot \varphi_0^2 [\vartheta_0 - \vartheta_s]^2}{4.575 T} \tag{8}$$

where V_S is the molar volume of the solid substance;

ϑ_0 is the known solubility parameter of the solvent;

φ_0 is the volumetric fraction of the solvent;

T is the abs. temperature, K;

x_s is the saturation molar fraction determined experimentally at temperature T;

x_s^i is the molar fraction (solid substance) in the case of ideal solubility,

ϑ_S is the unknown solubility parameter of the solid substance.

If the ideal solubility of the solid substance (x_s^i) at temperature T is known, the solubility parameter of the solid substance ϑ_S can be calculated from data x_s, φ_0 of a single experiment performed in a solvent of known solubility parameter ϑ_0.

The ideal solubility x_s^i of the substance at temperature T can be calculated from:

$$\lg x_s^i = -\frac{\Delta H_m}{4.575} \cdot \left[\frac{T_m - T}{T_m \cdot T}\right] + \frac{\Delta C_p}{4.575} \cdot \left[\frac{T_m - T}{T}\right] = \frac{\Delta C_p}{1.985} \lg \frac{T_m}{T} \tag{9}$$

where ΔH_m is the heat of melting;

T_m is the melting point, K;

ΔC_p is the difference between the molar heat capacity of the liquid and the solid substances, $C_p^1 - C_p^s$.

Since even the application of relationship (9) seems to be rather complicated, we tried to develop a simpler experimental procedure for the determination of the solubility parameter of solid substances.

By transposing Eq. (8) and by considering the values V_S and T as constant, the following relationship is obtained:

$$X_S = \frac{X_s^i}{A \cdot \varphi_0^2 (\vartheta_0 - \vartheta_s)^2} \,. \tag{10}$$

Disregarding the change of φ_0 and assuming the ideal solubility x_s^i to be constant, it can be established that the solubility of the solid substance, x_s, changes as a function of the solubility parameter ϑ_0 of the solvents used, according to a maximum curve. Maximum is located where the value of the exponential function is of unit value, thus:

$$\vartheta_0 = \vartheta_s \tag{11}$$

When condition (11) is fulfilled,

$$x_s^i = x_s, \tag{12}$$

the ideal solubility (which at the same time is the maximum solubility) is identical to the real solubility.

The experimental determination of the sought solubility parameter of the solid substance thus means essentially the determination of the saturation molar fraction of the solid substance x_S, at temperature T (expediently at 20 °C) in solvents of different but known and expediently selected solubility parameters ϑ_0, or, using Eq. (6), in two-component solvent mixtures. When the saturation molar fractions are plotted as a function of the solubility parameter ϑ_0 of the solvents (two-component mixtures) used, a maximum curve is obtained if the considerations have been realistic. The location of the maximum is the sought solubility parameter ϑ_S of the solid substance.

Experimental

Data of the solvent series of different solubility parameters used for the investigations are contained in Table I.

Table I

Data of the solvent series used for the investigations

No.	Name of the solvent	ϑ_0	M_0
1	Cyclohexane	8.20	84.06
2	Carbon tetrachloride	8.62	153.81
3	*o*-Xylene	9.00	106.08
4	Tetraline	9.50	132.20
5	1,2-Dichloroethane	9.80	98.92
6	Dichloromethane	10.04	84.91
7	*n*-Octanol	10.30	130.08
8	*s*-Butanol	10.80	74.04
9	*n*-Butanol	11.25	74.04
10	Isopropanol	11.50	60.03
11	*n*-Propanol	11.92	60.03
12	Ethanol	12.80	46.02
13	Methanol	14.48	32.01

Data of the solvents obtained by mixing solvent pairs, the proportions of mixing and the solubility parameters of the mixtures are contained in Table II. The general aim was to use solvents of low boiling point for the investigations. Experiments were carried out as follows:

Table II

Data of the solvent mixture series used for the investigations

Molar fractions of the components in the mixture		ϑ_0	H_0
n-Hexane	*Acetone*		
1.000	0.000	7.30	86.17
0.730	0.270	8.00	78.58
0.537	0.463	8.50	73.16
0.344	0.656	9.00	67.73
0.151	0.849	9.50	62.31
0.000	1.000	9.89	58.08
Acetone	*Methanol*		
1.000	0.000	9.89	58.08
0.867	0.133	10.50	54.61
0.758	0.242	11.00	51.79
0.649	0.351	11.50	48.95
0.541	0.459	12.00	46.08
0.431	0.569	12.50	43.27
0.322	0.678	13.00	40.44
0.214	0.786	13.50	37.61
0.105	0.895	14.00	34.53
0.000	1.000	14.48	32.04
Cyclohexane	*Ethanol*		
1.000	0.000	8.20	84.06
0.826	0.174	9.00	77.45
0.717	0.283	9.50	73.32
0.609	0.391	10.00	69.20
0.500	0.500	10.50	65.07
0.391	0.609	11.00	60.93
0.283	0.717	11.50	56.81
0.174	0.826	12.00	52.68
0.000	1.000	12.80	46.07

From the dry, pure solid substance, saturated solutions were prepared at 20 °C in solvents of different ϑ_0 values. From the saturated solutions portions of about 10 ml were taken, and the total weight $m_{\ddot{o}}$ of the solution was weighed on an analytical balance. The solution was cautiously evaporated to dryness, and the weight m_S of the solid residue was determined.

From these data the saturation molar fraction of the solid substance x_S has been determined by:

$$x_S = \frac{1}{1 + M_S[\alpha - 1] . K_S} \tag{13}$$

where $M_s =$ molecular weight of the dry, pure solid substance;

$K_s = 1/M_0$ where M_0 is the molecular weight of the solvent;

$\alpha = \dfrac{m_{\ddot{o}}}{m_s}$; and

$m_{\ddot{o}} =$ total weight of the solution;

$m_s =$ weight of the solid dry substance after evaporation.

The molar volume V_s of the solid substance (if the value of density ϱ_s is known, e.g. from determination by the saturation method):

$$V_s = \frac{M_s}{\varrho_s}. \tag{15}$$

The approximate value of the volume fraction of the solvent φ_0 in the solution investigated, assuming that the possible decrease in volume during dissolution is proportional to the volumes has been calculated as:

$$\frac{\dfrac{m_{\ddot{o}} - m_s}{\varrho_0}}{\dfrac{m_s}{\varrho_s} + \dfrac{m_{\ddot{o}} - m_s}{\varrho_0}} = \frac{\alpha - 1}{\alpha - 1 + \dfrac{\varrho_0}{\varrho_s}} \tag{16}$$

A few data of the solid substances of different structure investigated are contained in Table III. For all the substances the saturation molar fractions x_s have been determined at 20 °C in the solvents listed in Table I and in the solvent mixtures of the composition listed in Table II. Results of our investigations are shown on the example of N-isopropyl-chloroacetanilide (Table III, compund No. 7) in Fig. 1. For all the substances investigated, maximum curves similar to that shown by way of example have been obtained. From data in Table IV, the location of the maxima on the three curves is seen to be nearly identical.

According to data in Table IV, the deviations of the single measurements from the average of the three measurements, as the most probable value of ϑ_s, do not exceed in any of the cases ± 1.5. This result permits to conclude that the presumable solubility parameter ϑ_s of solid pesticides, compounds of pesticide type can be determined at an accuracy of ± 1.5 by the process described. On the other hand, in knowledge of the approximative value of the solubility parameter, the domain of solvents can be delimited, within which the best solvent is in all probability to be found. Moreover, the solubility parameter is suitable also for composing a solvent mixture of expectably favourable solution power [Eq. (6)].

Table III

Some characteristics of the compounds investigated

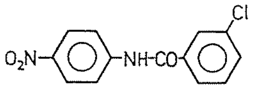
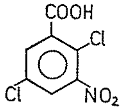
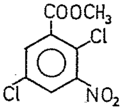
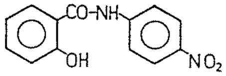
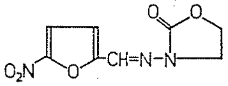
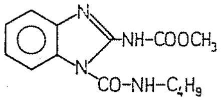
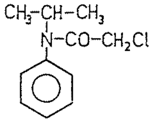
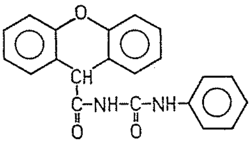
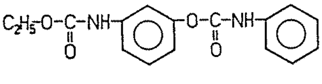
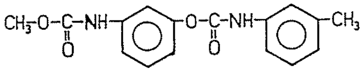
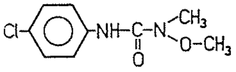
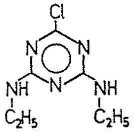
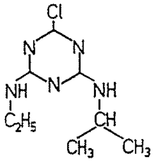
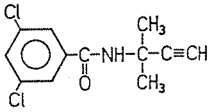
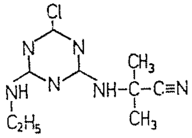
No.	Solid substances investigated		
	Structural formula	Density g/cm³	Melting point °C
1		1.62	227—229
2		1.66	215—220
3		1.42	69— 74
4		1.37	211—220
5		1.51	235—240
6		1.42	above 260
7		1.30	67— 76
8		1.19	225—227
9		1.38	113
10		1.45	145
11		1.27	74

Table III

No.	Solid substances investigated		
	Structural formula	Density g/cm³	Melting point °C
12		1.51	162
13		1.12	173—175
14		0.98	145
15		1.06	118—120

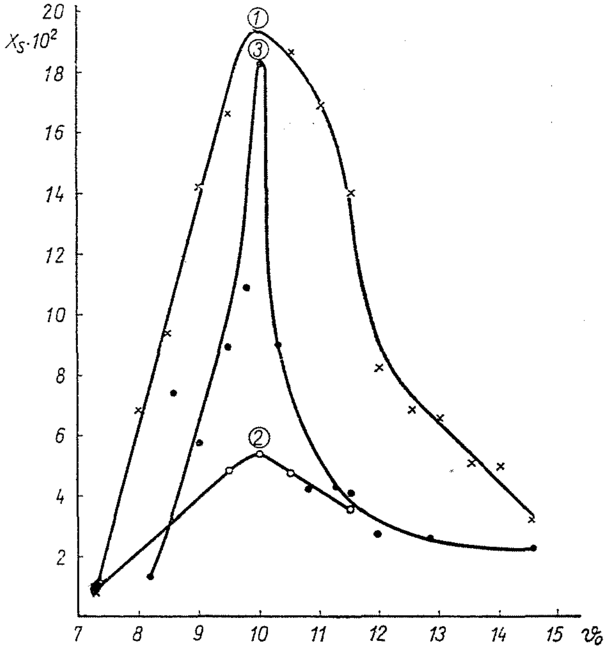


Fig. 1. Investigation of the solubility parameter of N-isopropyl-α-chloroacetanilide. 1. In n-hexane–acetone and acetone–methanol mixtures; 2. in cyclohexane–ethanol mixtures; 3. in solvent series

Table IV

Solubility parameter ϑ_S of the solid substances investigated

No. of the substance investigated according to Table III	Solubility parameter measured, ϑ_s				Deviation of the solubility parameter measured from the average, $\Delta\vartheta_s$		
	n-hexane-acetone, acetone-methanol	cyclohexane ethanol	solvent series	average			
	1	2	3	4	1	2	3
1	11.00	11.25	11.25	11.08	0.08	0.08	0.17
2	11.50	11.50	10.80	11.27	0.23	0.23	0.47
3	9.50	10.00	9.50	9.67	0.17	0.33	0.17
4	9.89	10.50	9.50	9.96	0.07	0.54	0.46
5	10.50	10.50	9.50	10.17	0.33	0.33	0.67
6	9.00	10.00	10.04	9.68	0.68	0.32	0.36
7	9.89	10.00	10.04	9.98	0.09	0.02	0.06
8	9.89	10.00	10.30	10.06	0.17	0.06	0.24
9	9.89	12.00	9.80	10.56	0.67	1.44	0.76
10	9.89	11.50	10.04	10.48	0.59	1.02	0.44
11	9.50	12.00	10.04	10.51	1.01	1.49	0.47
12	9.50	11.00	9.50	10.00	0.50	1.00	0.50
13	9.50	12.00	9.80	10.43	0.93	1.57	0.63
14	9.00	10.50	10.04	9.85	0.85	0.65	0.19
15	11.50	12.00	10.04	11.18	0.32	0.82	1.14

Summary

For the approximate, rapid evaluation of the solubility of compounds of solid pesticide type, it has been proved by investigations based on relationships relevant to the solubility parameter that the saturation molar fraction of solid substances changes as a function of the solubility parameter of suitably composed solvents and solvent mixtures according to a maximum curve. The values of maxima obtained in different investigations for the same substance are near identical. On the basis of these investigations the conclusion seems to be justified that the probable value of the solubility parameter ϑ_S of solid pesticides and compounds of pesticide type can be determined at an accuracy of ± 1.5 by the method of investigation described.

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