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The solubility parameter for biomedical polymers—Application of inverse gas chromatography

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ABSTRACT

The solubility parameter seems to be a useful tool for thermodynamic characterisation of different materials. The solubility parameter concept can be used to predict sufficient miscibility or solubility between a solvent and a polymer, as well as components of co-polymer matrix in composite biomaterials.

The values of solubility parameter were determined for polycaprolactone (PCL), polylactic acid (PLA) and polyethylene glycol (PEG) by using different procedures and experimental data, collected by means of inverse gas chromatography.

1. Introduction

In the design and preparation of various compositions or formulations, consisting of different components, the characteristics of these components, described by various physicochemical parameters, are important.

The application of the solubility parameter in the description of the behaviour of materials in real systems is presented including such phenomena as: miscibility, adhesion and wetting.

Hence, the suitable knowledge about mutual miscibility, solubility or compatibility between different materials is desirable. Understanding and quantification of interactions between the components of the system is very often a key problem. This allows to assess the suitability of compounds for established applications. One potential solution is to set the cohesive energy of the components, or more precisely, solubility parameter. This parameter is used for the estimation of the properties of an unknown material and the assessment of the interaction between different materials. The solubility parameter found an application for the prediction and correlation the cohesive and adhesive properties between different materials. It can be used in coatings industry for proper solvent selection in polymer/additives system [1,2] for characterisation of different additives (plasticisers, antistatic agents) used in polymers [3] matching a binder to pigment [4] in printing industry for selection of the best cleaning agent for binders [5].

Different polymers are currently investigated and used in biomedical field. Due to the unique properties of some polymers, such as e.g. biocompatibility or biofuncionality, their importance is constantly increasing.The solubility parameter concept can be used in all aspects of pharmaceutical dosage form design [6], for proper excipients selection [7,8] to predict the effectiveness of adhesives in dentine bonding systems and the ability of the resin to soften or solubilise the dentine surface [9–11], i.e. in characterisation of the materials applied in biological or biomedical systems. Moreover, the solubility parameter is one of the factors, which might be used to describe the penetration and absorption of various blood components into polymers, used as biomaterials [12]. It can be also applied to predict sufficient miscibility/solubility between solvent and polymer or components of co-polymer matrix in composite biomaterials.

The aim of this work was to estimate the solubility parameter data for polymers used as biomaterials: polycaprolactone, polylactic acid and polyethylene glycol. Polycaprolactone (PCL) is a semicrystalline, biocompatible, resorbable polymer, which found an application in biomedical field [13]. It is used as a component of composites in tissue engineering as a polymer for blood vessel and cartilage scaffolds [14], bone tissue regeneration [13–16], drug delivery systems [17] and others. Polylactic acid (PLA), due to its unique features of biodegradability, biocompatibility, thermoplastic processability and eco-friendliness, is the most common synthetic polymer used in medical applications, for scaffold preparation [18], in drug delivery systems [19], vascular grafts [20], implants for a bone fixation [21] etc. Poly(ethylene glycol) (PEG) is a commonly applied nonionic, hydrophilic polymer. The attach-

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ment of PEG chains has been employed as an effective method of choice in the development of biocompatible materials for many biological and biomedical applications [22].

The solubility parameter term is related to the cohesive energy density (CED), which indicates the energy of vaporisation per unit volume.

$$\delta = (CED)^{1/2} = \left[\Delta H - \left(RT/V_m\right)\right]^{1/2} = \left(\Delta E/V_m\right)^{1/2} \quad (1)$$

where: δ- solubility parameter, R – gas constant, T – temperature, ΔH – enthalpy of vaporisation, V_m – molar volume, ΔE – free energy of vaporisation.

The concept of the solubility parameter was proposed by Scatchard, Hildebrand and Scott and initially applied to systems, cohesion of which arises only from the dispersion forces. The solubility parameter, defined by Eq. (1) is called *Hildebrand solubility parameter* or *Hildebrand parameter* [23]. Its extension to system, where the cohesive energy can be considered as a sum of contributions from the dispersive (E_d), the polar (E_p) and the hydrogen bonding (E_h) was introduced by Hansen [2,3]:

$$-E_{coh} = -E_d - E_p - E_h \quad (2)$$

The so-called *Hansen solubility parameter* (HSP) is expressed as:

$$\delta_T^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \quad (3)$$

where: δ_T,δ_d, δ_p, δ_h denotes the total, the dispersive, the polar and the hydrogen bonding contribution, respectively.

The solubility parameter for volatile substances can be calculated from the energy of evaporation [24], by using Eq. (1), but this method gives only a total solubility parameter not Hansen solubility parameters. For low- or non-volatile compounds different methods were drawn up, e.g. solubility of a material in different solvents or a polymer swelling in different solvents, with known solubility parameters value. It is assumed, that the solubility parameter of the investigated material is approximately the same as the solubility parameter of the solvent, which dissolves this material or mixes with it at all proportions, without a change of volume and enthalpy [25]. A similar method is the measurement of the polymer swelling in solvents with known solubility parameter value, taken from literature [26]. Different group contribution methods, e.g. the Hoftyzer and Van Krevelen method can be applied to calculate the solubility parameter, knowing the chemical structure of a material [26–29]. It is assumed, that two materials, having close values of the solubility parameter are likely to be compatible and should be miscible, when mixed together.

In this work, inverse gas chromatography was applied for the determination of the solubility parameter for polymers used in biomedical applications. Inverse gas chromatography (IGC) is known as an effective technique to measure different physicochemical parameters and it allows to calculate the solubility parameter, for a wide range of low- or non-volatile materials in a large range of temperatures. In the IGC technique, an investigated material (a stationary phase) is placed in the chromatographic column, and its properties are deduced from behaviour of injected, volatile probes (test solutes), transported by a mobile phase. As a result of an interaction between the test solutes and the stationary phase, the retention data obtained are used to calculate the Flory-Huggins interaction parameter ($\chi_{1,2}^{\infty}$) and furtherly the solubility parameter (δ_2) [30].

The interaction parameter is considered as the Gibbs free energy parameter and such assumption allows dividing the interaction parameter $\chi_{1,2,}^{\infty}$ into the enthalpy χ_H^{∞} and the entropy χ_S^{∞} components [31,32]:

$$\chi_{1,2}^{\infty} = \chi_H^{\infty} + \chi_s^{\infty} \quad (4)$$

and is related with the solubility parameter by [31]:

$$\chi_{1,2}^{\infty} = (V_1/RT)(\delta_1 - \delta_2)^2 + \chi_s^{\infty} \quad (5)$$

where δ_1 and $\delta_2$are the solubility parameter of the test solvent and the investigated material, respectively and V_1 is the solvent molar volume.

The injected test solute is absorbed in the stationary phase (the investigated material). The knowledge of the retention of the test solute, expressed as the specific retention volume, allows to calculate the interaction parameter [32]:

$$\chi_{(1,2)i}^{\infty} = \ln\left(273.15R/p_1^0 V_g M_1\right) - p_1^0/RT\left(B_{11} - V_1^0\right) - 1 \quad (6)$$

where *1* denotes the solute and *2* denotes the examined material, M_1, p_1^0, B_{11}, V_g,V_1^0 are the molecular mass, the saturated vapour pressure of the test solute, the second virial coefficient of the test solute, the specific retention volume of the test solute and the molar volume of the test solute, respectively.

Smidsrod and Guillet were the first to apply the inverse gas chromatography to research the interactions between a solvent and a polymer as a stationary phase. The method of determination is based on the rule, that the Flory-Huggins parameter, obtained from the retention data, can be related to the solubility parameter by the Eq. (5). Ito and Guillet [32] proposed to estimate the solubility parameter of polymers, having a set of $\chi_{(1,2)i}^{\infty}$ and δ_{1i} values for the respective test solutes, by using the equation:

$$\delta_{1i}^2/RT - \chi_{(1,2)i}^{\infty}/V_1^o = (2\delta_2/RT)\delta_{1i} - \left(\delta_2^2/RT + \chi_s^{\infty}/V_i\right) \quad (7)$$

The slope of linear relationship $\left(2\delta_2/RT\right)$ versus δ_{1i} is proportional to the solubility parameter of the examined material, i.e. δ_2 [32–37].

The value of δ_2 can also be calculated from:

$$intercept = \left(\delta_2^2/RT + \chi_s^{\infty}/V_i\right) \quad (8)$$

assuming χ_s^{∞} = 0.2; 0.3 or 0.4 and taking for V_i the smallest molar volume of the test solute.

The Guillet procedure was used by Price [38] to determine the solubility parameter for the compounds with small molecular mass. He described the solubility parameter as a sum of two factors arising from the dispersive and the polar interactions between the investigated material and the test solute:

$$\delta_T^2 = \delta_d^2 + \delta_p^2 \quad (9)$$

Voelkel and Janas [34] extended the test solute group in order to estimate the three-parameter Hansen equation. The division of the test solutes into groups, corresponding to different types of intermolecular interactions, enables the dispersiveδ_d, the polar δ_p and the hydrogen bonding δ_h components of the total solubility parameter value to be obtained, according to the relations:

$$\delta_d = \frac{m_{n-alkanes} \times RT}{2} \quad \text{a)}$$

$$\delta_p = \frac{(m_1 - m_{n-alkanes}) \times RT}{2} \quad \text{b)} \quad (10)$$

$$\delta_h = \frac{(m_2 - m_{n-alkanes}) \times RT}{2} \quad \text{c)}$$

where $m_{n-alkanes}$ – the value of the slope for n-alkanes; m_1 – the value of the slope for aromatic hydrocarbons, ketones, 1-nitropropane; m_2 – the value of the slope for alcohols and pyridine.

The alternative procedure for estimation the polymers solubility parameter is linked to the assumption, presented by Lindvig et al. [39]. They proposed using the modified Hansen relationship, correlating the experimentally determined values of the Flory-Huggins