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Characterization of Hybrid Materials by means of Inverse Gas Chromatography and Chemometrics

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ABSTRACT

The surface properties of hybrid materials (potential carriers for sustained release of active agents) have been examined by inverse gas chromatography (IGC). A nonsteroidal anti-inflammatory agent – ibuprofen was used as a model for active compound. The following parameters have been used to characterize the interactions between the constituents of the hybrid material and the active agent: dispersive component of the surface free energy γ_S^D, K_A and K_D parameters describing the acidity and basicity, respectively, and Flory-Huggins parameter $\chi_{23}^{'}$ (the magnitude of interactions). Principal component analysis (PCA) and the procedure based on sum of ranking differences (SRD) were applied for selection of hybrid materials and parameters for characterization of these materials. One loose cluster found by PCA grouping of hybrid materials is refined by SRD analysis: SRD grouping indicates three groups having somewhat dissimilar properties.

Keywords

Physicochemical properties, solid dosage form, biodegradable polymers, drug carrier, surface chemistry, hybrid materials, inverse gas chromatography, principal component analysis, chemometrics

INTRODUCTION

Hybrid materials are formed by the combination of polymers and inorganic solids on the molecular scale. The structure and properties that can be obtained for hybrid materials depend on the chemical nature of their chemical components. The character of these components and interactions between the organic and inorganic part have been used to categorize these hybrid materials into two classes. Class I contains materials with week chemical bonding such as hydrogen bonding, van der Waals contacts or electrostatic forces. Class II corresponds to strong chemical interactions between components like covalent or ionic-covalent bonds.[1,2] The most important advantage of hybrid material is connecting of dissimilar properties of individual components leading to new properties not accessible otherwise that make them suitable for a wide range of medical application. There is a definite need to use hybrid materials as carriers in the pharmaceutical dosage forms and in the future implementation to the pharmacy. They are widely used for bone tissue engineering that fulfill the clinical demands.[3] The properties such as biocompatibility and biodegradability open new prospects for these materials with special incidence to sustained release of drugs.[4] Creating hybrid materials for use in sustained release formulations of active agent is the primary direction of research to develop new dosage forms. Selection criterion depends on the interaction between their individual components and its physicochemical properties.

In the last few years the biomedical research has shown growing interest towards bioceramics. Inorganic material can act as a matrix and it is able to host organic molecules, such as drugs. There are some weak interaction between the host inorganic matrix and the guest drug (the organic component).[5,6] Among bioceramics, silica is popular due to their capability to host different molecules. Fumed silica has small particle size and large surface area. Three chemical groups are present on the surface of fumed silica: isolated hydroxyl, hydrogen-bonded hydroxyl and siloxane groups. Generally, the surface is hydrophilic, while the

siloxane groups are hydrophobic.[7] Biodegradable polymers are frequently applied as organic materials due to the fact that products of their metabolic processes are completely removable and non-toxic.[8]

Many experiments including physicochemical tests should be carried out to implement a new hybrid material as excipient to pharmaceutical use. Inverse gas chromatography (IGC) will be particularly useful in this case. This is a new application for the investigation of physicochemical properties of materials as drug carriers. This method can be helpful in understanding the changes in hybrid materials by various pharmaceutical processes.[9] The examined material is placed in the chromatographic column. The test solutes are injected into the flow of carrier gas and transported over the surface of the examined material. The retention times of test solutes results from the interactions between solute and stationary phase (examined material). These retention data are further applied to estimate the properties of material of interest.

The retention times can be used for the determination surface activity by determination of γ_S^D, the dispersive component of the free surface energy; the acidity and basicity of the surface (K_A and K_D parameters) and $\chi_{23}^{'}$ Flory-Huggins interaction parameters expressing the strength of interactions between the constituents of the hybrid material.[10,11] The reversed-flow gas chromatography (RFGC) is a version of IGC and RFGC has been successfully applied (i) for the measurement of the dispersive component of surface free energy, (ii) for the determination of Flory-Huggins interaction parameters and (iii) for that of solubility parameters in polymer-solvent systems.[12,13]

The aim of this study was the characterization of hybrid materials by inverse gas chromatography and application chemometrics to select one group of materials, which could be used as drug carrier.

Some computer programs Statistica (StatSoft, Inc. (2005). STATISTICA (data analysis software system), version 7.1. www.statsoft.com.), and CRRN-SRD allow assessing the quality of results including the separation of the parameters most relevant to the studied

phenomenon. Experimental data were analyzed by principle component analysis (PCA) and a procedure based on sum of ranking differences (SRD). These methods allow finding similarities and dissimilarities among various hybrids materials.

EXPERIMENTAL

Materials

Preparation of ternary hybrid materials with incorporation of the active agent was achieved by the sorption of ibuprofen on silica and evaporation of the solvent. Aerosil 200V and Aerosil 816 were purchased from Degussa (Darmstadt, Germany), microcellulose from Rettenmaier (Weibenborn, Germany) were used as supporting base for hybrid materials. The organic constituent of hydrid material was obtained by using one of the following polymers: poly ethylene glycol (PEG 10000), poly(L-lactide) were supplied by Fluka, Pluronic F127 (Sigma Aldrich, Poznań, Poland). Ibuprofen was obtained from Polpharma (Poznań, Poland). Hybrid systems contain individual specimens in different proportions (w/w). The amount of ibuprofen in hybrid material was equal to 200mg. Examined materials are presented in Table 1.

IGC experiments

IGC measurements were carried out with the use of IGC SMS Ltd. gas chromatograph equipped with a thermal conductivity detector (TCD) and a flame-ionization detector (FID). Carrier gas was dry helium with flow rate 15.0 mL/min. Each column was made from glass, I.D. 4 mm, length 30 cm were used. The measurements were carried out at 37 ^{o}C, injector and detector temperature was equal to 150 ^{o}C. The column filling was prepared by covering glass beads with the powder to obtain homogeneous layer of the examined material. The columns were conditioned 2 h at the temperature and flow-rate used during IGC experiment. As test solutes were used:

- nonpolar compounds: hexane purity 99% (Chempur, Tarnowskie Góry, Poland) C_6, heptane purity 99% (Sigma Aldrich, Poznań, Poland) C_7, octane purity 99% (Fluka, Poznań, Poland) C_8, nonane purity 99% (Acros Organics, Gliwice, Poland) C_9;
- polar compounds: chloroform analytical grade (POCH S.A., Gliwice, Poland) $CHCl_3$, ethanol purity 99% (POCH S.A., Gliwice, Poland) EtOH, 1,4-dioxane purity 99% (Fluka, Poznań, Poland) $C_4H_8O_2$, acetonitrile analytical grade (POCH S.A., Poland) ACN and ethyl acetate HPLC grade (POCH S.A., Gliwice, Poland) $CH_3COOC_2H_5$.

Parameters describing surface properties of hybrid materials were calculated from the retention data of test solutes injected into a column with examined material played a role of stationary phase.

The dispersive component of the free surface energy γ_S^D was determined by two methods: Dorris-Gray and Schultz-Lavielle.[14-16] In case of Schultz-Lavielle method γ_S^D parameter was calculated based on equation:

$$R \cdot T \cdot \ln V_N = 2 \cdot N \cdot a \cdot \sqrt{\gamma_S^D \cdot \gamma_L^D} + C \qquad (1)$$

where: R – the gas constant, 8.314 [J/(mol·K)]; T – the absolute temperature of measurement [K]; V_N - net retention volume [m^3]; N – the number of Avogadro, $6.023 \cdot 10^{23}$ [1/mol]; a – cross sectional area of the adsorbate [m^2]; γ_S^D - the dispersive component of surface free energy [mJ/m^2]; γ_L^D - the dispersive component of the surface tension of the test solute in liquid state [mJ/m^2]; C – constant.

The straight line relationship: left-hand side of eq. (1) *vs.* $a \cdot \sqrt{\gamma_L^D}$ for *n*-alkanes series allows calculating γ_S^D from the slope value.

According to the method of Dorris and Gray, γ_S^D was calculated from the equation:

$$\gamma_S^D = \frac{[R \cdot T \cdot \ln(V_N^{(C_{n+1}H_{2n+4})}) / (V_N^{C_nH_{2n+2}})]}{4 \cdot N^2 (a_{CH_2})^2 \gamma_{CH_2}} \qquad (2)$$

where: $V_N^{(C_{n+1}H_{2n+4})}$ is the net retention volume of $C_{n+1}H_{2n+4}$ and $V_N^{(C_nH_{2n+2})}$ is the net retention volume of C_nH_{2n+2}; a_{CH_2} is the surface area of a methylene group [m^2]; γ_{CH_2} is the surface energy of polyethylene-type polymers with a finite molecular mass [mJ/m^2].

K_A and K_D parameters express acidity and basicity of the surface layer of the examined material. They are related to the energy of specific interaction (ΔG_{sp}) between the examined surface and the test solute.[17,18] The parameters were determined from equation:

$$\frac{\Delta G_{sp}}{AN^*} = \frac{DN}{AN^*} \cdot K_A + K_D \tag{3}$$

where K_A is the parameter expressing acidic properties of solid surface; K_D is the parameter expressing basic properties of solid surface; ΔG_{sp} is the specific component of free energy of adsorption of polar compound; DN is the donor number of the polar test solute; AN^* is the acceptor number of the polar test solute.

The magnitude of interaction between the test solute (1) and examined material (*j*) might be expressed by the value of Flory-Huggins interaction parameter, χ_{12}^{∞}:[19]

$$\chi_{1j}^{\infty} = \ln\left(\frac{273{,}15R}{P_1^o \cdot V_g^o \cdot M_1}\right) - \frac{P_1^o}{RT}\left(B_{11} - V_1^o\right) + \ln\frac{\rho_1}{\rho_j} - \left(1 - \frac{V_1^o}{V_j^o}\right) \tag{4}$$

where *j* - examined material, M_1 is the molecular mass of the solute, p_1^o is the saturated vapor pressure of the solute, B_{11} is the second virial coefficient of the solute, V_1^o and V_j^o are the molar volumes of the test solute and examined material, respectively, ρ_1 and ρ_j are the densities of the test solute and examined material, respectively, V_g^o is specific retention volume and R is the gas constant.

It is also possible to quantify the magnitude of interaction between constituents of complex material was expressed using Flory–Huggins parameter χ_{23}':[20,21]

$$\chi'_{23} = \frac{1}{\phi_2 \cdot \phi_3}(\chi^{\infty}_{12} \cdot \phi_2 + \chi^{\infty}_{13} \cdot \phi_3 - \chi^{\infty}_{1m}) \quad (5)$$

where χ^{∞}_{1m} denote the Flory–Huggins interaction parameter for test solute/hybrid material pair while $\chi^{\infty}_{12}, \chi^{\infty}_{13}$ are Flory-Huggins parameters for test solute/component (2 or 3) pairs; ϕ_2 and ϕ_3 denote volume fraction of component in examined material.

Principal Component Analysis, PCA

Supposing that there exists some latent structure in the input data matrix, its dimensions were reduced using principal component analysis as given elsewhere.[22-24] The principal components are calculated such that they should be uncorrelated and should account for the total variance of original variables. The first principal component should account for a maximum of the total variance; the second principal component should be uncorrelated with the first one and should account for a maximum of the residual variance, and so on until the total variance is accounted for. Usually, it is sufficient to retain only a few components accounting for a large percentage of the total variance. PCA will show, which hybrid materials and which test solutes are similar, i.e. carry comparable information and which one is unique.[24-25]

PCA is particularly useful for pattern recognition of IGC data and show similarities and differences between them. PCA give information which objects or variables are unique.[25]

Sum of ranking differences (SRD)

Sum of ranking differences based on comparison of absolute differences in rank numbers. In this method the absolute values of differences between reference and individual rankings are calculated and summed for each variable. Such a way all hybrid materials can be compared:

each of them receives an SRD values. The less discrepancy of SRD values shows similarity of the variables. The outliers can also be observed, where distance shows dissimilarity.[26,27]

RESULTS AND DISCUSSION

The hybrid materials were characterized by surface parameters. The values of dispersive component of free surface energy, γ_S^D, K_A and K_D parameters of examined materials and their single components are summarized in Table 1. Standard deviation for γ_S^D equals ± 2 mJ/m^2, the same both for K_A and K_D parameters are ± 0.01, and for χ'_{23} ± 0.009.

One grouping of hybrid materials can be observed in Figure 1. However, there are outliers from the rest. As seen in all projections, single components of hybrid material stand out e.g. A - Aerosil 816, B - Aerosil 200V, PEG – polyethylene glycol, IB – ibuprofen. Some materials also exhibit slight differences from the other ones like: B1 – Aerosil 200V+IB (10:1) and two hybrid system A3 – Aerosil 816+IB+PLU (1:1:1) and B8 – Aerosil 200V+IB+PLA (10:1:10). Analysis of scatterplots indicates a high degree of similarity of surface parameters for hybrid materials. One may suggest the replacement of a given hybrid material by another one exhibiting similar activity. It might enable the selection of various materials having the same or very similar.

Much higher expectations can be associated with Flory-Huggins parameter χ'_{23}.

The magnitude of Flory-Huggins parameter between the components of hybrid material will probably depend on their chemical structure of polymeric component and amount of both, organic and inorganic part in the system. However, the analysis (evaluation) of relationship between χ'_{23} value on the type of test solute used in IGC experiment is a hard task. This is well known problem in IGC literature.[21,28,29]

Values of Flory-Huggins interaction parameter for hybrid materials are collected in Table 2.

Plot of eigenvalues clearly demonstrates that three principal components (PCs) satisfactorily describe the variability of values of Flory-Huggins parameters (Figure 2). Three principal components explained more than 93% of total variance in the data. Solely the first and second principal components explained more than 80% of total variance in data. Please do note, that PCs values are different from that presented in Figure 1. These earlier were calculated for experimental data collected in Table 1, i.e. for surface parameters determined by means of IGC. PCs presented in Figures 2, 3 and 4 were derived for Flory-Huggins parameter from Table 2.

Results presented in Figure 3 suggest the possibility for elimination of some test solutes. Values of Flory-Huggins parameter for C_6, C_7, C_8, C_9 show high similarities as well as $CHCl_3$, $C_4H_8O_2$ and EtOH or ACN with $CH_3COOC_2H_5$. Therefore, there is no need to use all of these test solutes for the given characterization of a hybrid material. Thus, solvent grouping can reduce the amount of test solutes and select one representative solvent from each group. However, the clustering of materials is preserved.

Values of Flory-Huggins parameters might be used for selection of examined materials. It would be interesting to group the examined materials according to their magnitude of interactions between constituents of hybrid materials – indicating their similarity or dissimilarity. This task may be solved by using of PCA as presented in Figure 4. This grouping of hybrid materials leads to the selection of only one loose cluster. Hybrid materials show similarity among each other. However, regardless of projections (Figures 4a-4c) some materials exhibit somewhat different properties than other ones, e.g.: A3, B4, B7, B8, M3. Maybe these distinguished individuals will be better carriers for active agent release. Better carrier means here such one, for which ibuprofen release remains on the effective level for a longer time. Other hybrid materials are characterized by close values of χ'_{23} what indicates

similar interaction levels between the constituents. In such a case the type and amount of polymers do not significantly influence the properties, here – the ability to drug release.

Sum of Ranking Differences

The average the value of Flory-Higgins parameters (row average) has been used as benchmark for ranking. Three main groups can be observed – hybrid materials: cluster 1: B3, B4, B5, B6, B7; cluster 2: A2, A4, B8 and cluster 3: M2, M3, A3 (Figure 5).

The hybrid material most similar to the average of all hybrid materials is denoted by B4 and the most dissimilar one is denoted by M2. B2 rather differs individually. The SRD ranking indicates that B4 should be chosen as a good candidate to replace all the other hybrid materials. If a most "dissimilar" hybrid material is to be selected, than M2 is the best choice. Selection of M2 does not necessarily mean that e.g., this hybrid material has the highest magnitude of interactions between constituents of materials, but the results will be most different from those of the other hybrid materials, if these ones were used. It is easy to find a replacement of hybrid material, as B5 and B6 are (almost) equivalent; closeness on the SRD scale also shows similarity: B7 can be replaced by B5 or B6. Obtaining as different results for hybrid material as possible B4 can be replaced by M3.

CONCLUSION

IGC provides information on physicochemical properties of hybrid materials and interaction between their constituents. The values of dispersive component of the free surface energy γ_S^D, K_A and K_D parameters indicate moderate activity of examined materials. Negative values of Flory-Huggins parameter χ'_{23} shows moderate magnitude of interaction between components of examined materials. PCA makes possible the significant reduction of the number of test solutes required for the determination of Flory–Huggins parameter. Factor loading plots show

that there is no need to use all of the interaction parameters. Several of these parameters carry out very similar information. Majority of investigated hybrid materials exhibit similar physicochemical characteristics, what is indicated by the presence of a loose cluster in Figure 4. However, some individuals can also be found in this group. SRD analysis refines the grouping and indicates three sub-groups of hybrid materials having somewhat dissimilar properties.

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REFERENCES:

1. Ashby MF, Brechet YJM. 2003. Designing hybrid materials. Acta Mater 51:5801-5821.

2. Hoffmann F, Cornelius M, Morell J, Fröba M. 2006. Silica-based mesoporous organic-inorganic hybrid materials. Angew Chem Int Ed 45:3216-3251.

3. Costa VC, Costa HS, Vasconcelos WL, Pereira MM, Oréfice RL, Mansur HS. 2007. Preparation of hybrid biomaterials for bone tissue engineering. Mater Res 10:21-26.

4. Jesson DA, Abel ML, Hay JN, Smith PA, Watts JF. 2006. Organic-Inorganic Hybrid nanoparticles: Surface Characteristics and Interactions with a Polyester Resin. Langmuir**,** 22:5144-5151.

5. Fengyu Qu, Huiming Lin, Xiang Wu, Xiaofeng Li, Shilun Qiu, Guangshan Zhu. 2010. Bio-templated synthesis of highly ordered macro-mesoporous silica material for sustained drug delivery. Solid State Sci 12:851-856.

6. Manzano M, Vallet-Regi M. 2010. New developments in ordered mesoporous materials for drug delivery. J Mater Chem 20:5593-5604.

7. Arruebo M. 2012. Drug delivery from structured porous inorganic materials. Wiley Interdiscip Rev Nanomed Nanobiotechnol 4:16-30.

8. Gareth A, Hughes PhD. 2005. Nanostructure-mediated drug delivery. Nanomed Nanotechnol 1:22-30.

9. Das SC, Stewart PJ. 2012. Characterising surface energy of pharmaceutical powders by inverse gas chromatography at finite dilution. J Pharm Pharmacol 64:1337-1348.

10. Papadopoulou SK, Panayiotou C. 2012. Thermodynamic characterization of poly(1,1,1,3,3,3-hexafluoroisopropyl methacrylate) by inverse gas chromatography. J Chromatogr A 1229:230-236.

11. Voelkel A, Strzemiecka B, Adamska K, Milczewska K. 2009. Inverse gas chromatography as a source of physiochemical data. J Chromatogr A 1216:1551-1566.

12. Katsanos NA, Karaiskakis G. 1987. Analytical applications of reversed-flow gas chromatography. Analyst 112: 809-813.

13. Agathonos P, Karaiskakis G. 1989. Thermodynamic study of polymer solvent systems by reversed-flow gas chromatography. J Appl Polym Sci 37:2237-2250.

14. Belgacem MN, Gandini A. 1999. Inverse Gas Chromatography as a tool to characterize dispersive and acid-base properties of the surface of fibers and powders. In Pefferkorn E, editor. Interfacial Phenomena In Chromatography. New York: Marcel Dekker Inc. p. 41-124.

15. Grimsey IM, Feeley JC, York P. 2002. Analysis of the surface energy of pharmaceutical powders by inverse gas chromatography. J Pharm Sci 91:571-583.

16. Schultz J, Lavielle L, Martin C. 1987. The role of the interface in carbon fibre-epoxy composites. J Adhesion 23:45-60.

17. Bilgiç C, Tümsek F. 2007. Determination of the acid/base properties of MgY and NH_4Y molecular sieves by inverse gas chromatography. J Chromatogr A 1162:83-89.

18. Hajdar H, Balard H, Papirer E. 1995. An inverse gas chromatography study of crystalline and amorphous silicas. Colloid Surface. 99:45-51.

19. Huang JCh., Deanin RD. 2004. Concentration dependency of interaction parameter between PVC and plasticizers using inverse gas chromatography. J Appl Polym Sci 91:146-156.

20. Al-Saigh ZY. 1997. Inverse gas chromatography for the characterization of polymer blends. Int J Polym Anal Charact. 3:249-291.

21. Milczewska K, Voelkel A. 2012. Inverse Gas Chromatography in Characterization of Composites Interaction. In Mohd MA, editor. Advanced Gas Chromatography - Progress in Agricultural, Biomedical and Industrial Applications, Rijeka: InTech p. 421-436.

22. Forlay-Frick P, Fekete J, Héberger K. 2005. Classification and replacement test of HPLC systems using principal component analysis. Anal Chim Acta 536:71-81.

23. Pasadakis N, Yiokari C, Varotsis N, Vayenas C. 2001. Characterization of hydrotreating catalysts using the principal component analysis. Appl Catal A 207:333–341.

24. Otto M. 1999. Chemometrics, Statistics and Computer Application in Analytical Chemistry. Weinheim: Wiley-VCH.

25. Wold S, Esbensen K, Geladi P. 1987. Principal Component Analysis. Chemometr. Intell. Lab. Syst. 2:37-52.

26. Héberger K. 2010. Sum of ranking differences compares methods or models fairly. Trends Anal Chem, 29: 101-109.

27. Héberger K, Kollár-Hunek K. 2011. Sum of ranking differences for method discrimination and its validation: Comparison of ranks with random numbers J Chemometrics 25:151-158.

28. Fernandez-Sanchez E, Fernandez-Torres A, Garcia-Dominguez JA, Santiuste JM, Pertierra-Rimada E. 1988. Solubility parameters of gas chromatographic mixed stationary phases. J Chromatogr 457:55-71.

29. Farooque AM, Deshpande DD. 1992. Studies of polystyrene-polybutadiene blend system by inverse gas chromatography. Polymer 33:5005-5018.

Figure legend:

Figure 1. Results of principal component analysis for surface parameters. Different two-dimensional projections of PCs; explained variances are in brackets.

Figure 2. Plot of eigenvalues against their serial numbers.

Figure 3. Results of principal component analysis for Flory-Huggins parameters: A characteristic projection of factor loadings (PC1 *vs.* PC3).

Figure 4. Results of principal component analysis for Flory-Huggins parameters: several two-dimensional projections of factor scores (PC1 *vs.* PC2 and PC1 *vs.* PC3 as well as PC2 *vs.* PC3).

Figure 5. Grouping by sum of ranking differences. Scaled SRD values (between 0 and 100) are plotted on the x axis and left y axis. Relative frequencies for Gaussian like theoretical distribution are seen on the right y axis (XX1 – 5% Med – median XX19 – 95%).

Table 1. Values of dispersive component of free surface energy, K_A and K_D parameters of examined hybrid materials and their single components.

Hybrid materials	**Proportions**	**Notation**	γ_S^D **by Dorris-Gray metod**	γ_S^D **by Schultz-Lavielle metod**	K_A	K_D	K_A/K_D
Aerosil 816	**-**	**A**	35.5	29.2	0.185	0.038	4.86
Aerosil 200V	**-**	**B**	75.6	59.6	0.160	0.075	2.20
Ibuprofen	**-**	**IB**	39.0	36.4	0.103	0.07	1.47
Poly ethylene glycol	**-**	**PEG**	41.4	37.7	0.073	0.494	0.15
Poly lactid acid	**-**	**PLA**	48.4	44.6	0.137	0.119	1.15
Pluronic F127	**-**	**PLU**	53.5	46.2	0.130	0.243	0.53
Microcelulose	**-**	**M**	37.5	37.3	0.181	0.211	0.86
A+IB	**1:1**	**A1**	37.7	35.2	0.087	0.113	0.77
AR+IB+PEG	**1:1:1**	**A2**	47.1	43.0	0.104	0.110	0.94
AR+IB+PLA	**1:1:1**	**A3**	34.7	32.4	0.109	0.054	2.02
AR+IB+PLU	**1:1:1**	**A4**	40.4	37.5	0.143	0.229	0.62
M+IB	**1:1**	**M1**	41.1	38.9	0.183	0.220	0.83
M+IB+PLA	**1:1:1**	**M2**	35.7	34.9	0.142	0.126	1.13
M+IB+PLU	**1:1:1**	**M3**	47.2	45.0	0.116	0.249	0.46
B+IB	**1:1**	**B1**	35.8	34.9	0.040	0.514	0.07
B+IB+PEG	**10:1:10**	**B2**	34.9	32.2	0.143	0.138	1.04
B+IB+PEG	**10:1:5**	**B3**	33.3	30.4	0.145	0.168	0.86
B+IB+PEG	**10:1:2**	**B4**	35.2	31.4	0.136	0.158	0.86
B+IB+PLU	**10:1:10**	**B5**	48.7	44.2	0.164	0.269	0.61
B+IB+PLU	**10:1:5**	**B6**	38.2	34.3	0.143	0.169	0.84
B+IB+PLU	**10:1:2**	**B7**	48.4	44.7	0.124	0.256	0.48
B+IB+PLA_	**10:1:10**	**B8**	32.9	37.0	0.226	0.121	1.86

Table 2. Values of Flory-Huggins parameter of examined hybrid materials.

Materials	C_6	C_7	C_8	C_9	$CHCl_3$	EtOH	$CH_3COOC_2H_5$	ACN	$C_4H_8O_2$
B2	-3.215	-1.701	-0.537	0.537	2.429	-0.532	-3.708	-0.207	0.873
B3	-3.052	-0.311	-3.625	-4.035	-3.605	-5.552	-12.106	-8.097	-0.286
B4	-9.205	-2.956	-9.963	-10.33	-6.03	-13.09	-24.293	-15.92	-0.886
B5	3.216	7.631	-2.081	-1.725	2.135	-2.005	-6.223	-2.676	1.561
B6	-0.293	4.269	-5.188	-5.299	-1.968	-4.258	-11.408	-6.569	0.266
B7	-0.999	1.224	-3.242	-3.098	6.769	-2.094	-14.986	-11.06	9.375
B8	1.979	3.453	1.937	1.659	4.039	-0.846	3.765	-1.425	13.996
A2	-5.083	-4.882	-4.711	-3.827	-9.245	-10.21	-11.111	-10.90	-8.409
A3	-13.87	-19.34	-6.041	-5.972	-3.204	0.008	-6.521	0.929	-3.122
A4	-4.993	-4.828	-4.846	-4.137	-4.663	-14.30	-7.402	-9.739	-3.925
M2	1.359	4.19	0.854	0.272	0.103	3.201	1.05	5.561	0.588
M3	8.205	7.764	4.496	4.598	5.727	6.385	3.733	15.118	3.593

Figure 1

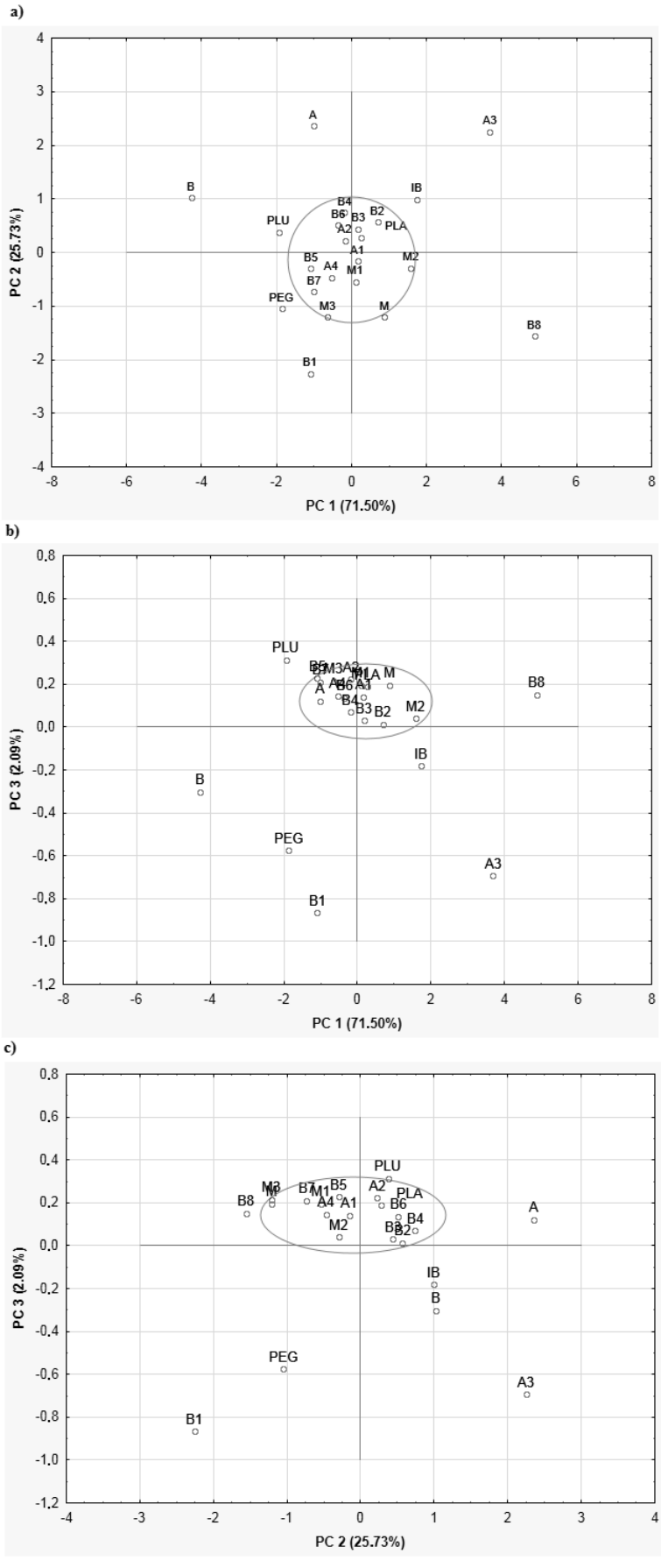

a)
PC 2 (25.73%)
PC 1 (71.50%)
A
A3
B
IB
PLU
PLA
A2
A1
M2
A4
M1
B5
B7
PEG
M3
M
B8
B1
b)
PC 3 (2.09%)
PC 1 (71.50%)
PLU
M
B8
M2
IB
B
PEG
A3
B1
c)
PC 3 (2.09%)
PC 2 (25.73%)
PLU
PLA
A
IB
B
PEG
A3
B1

Figure 2

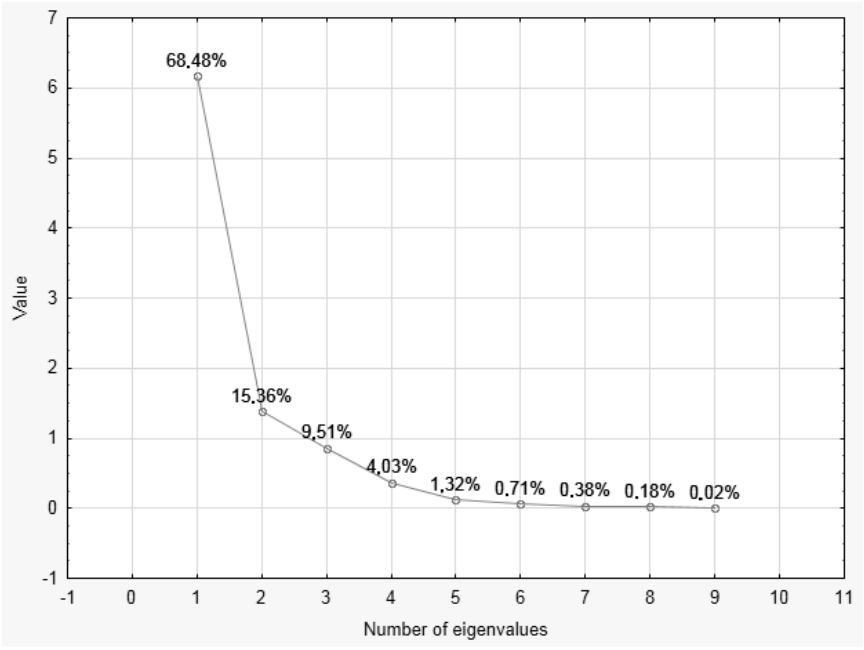


Figure 3

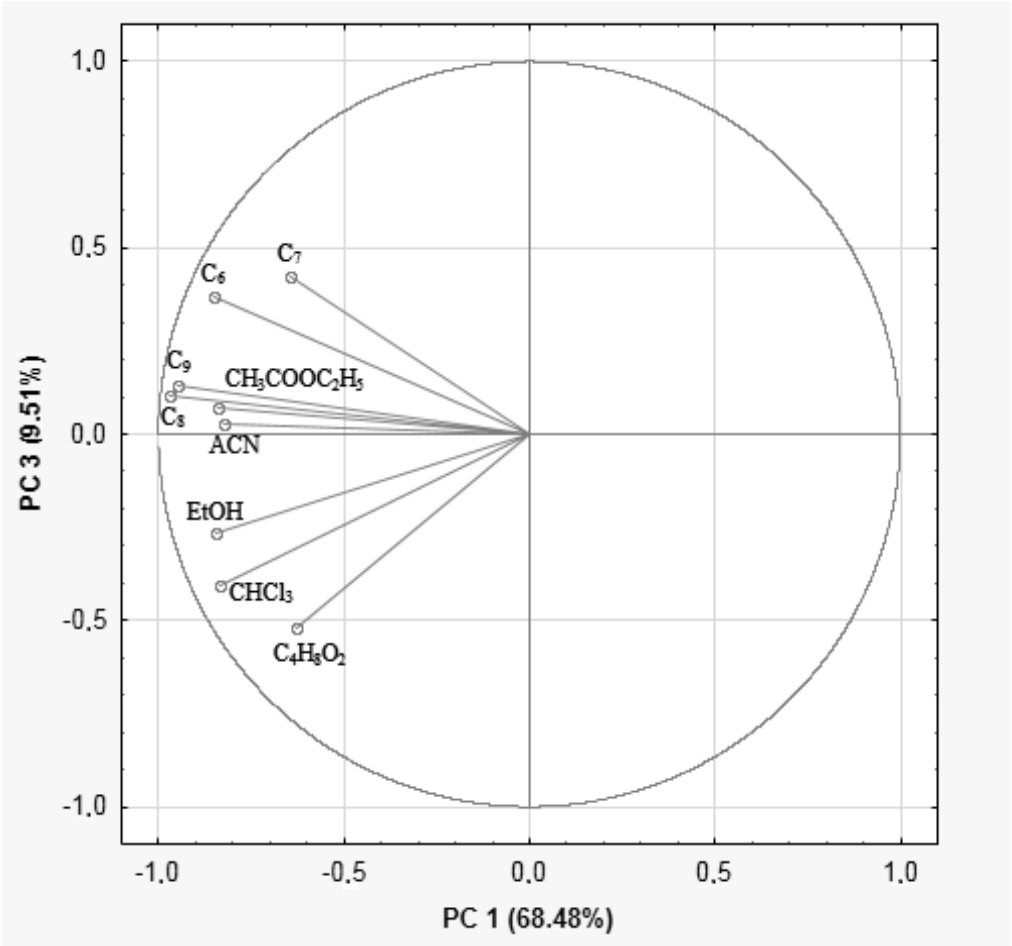


Figure 4

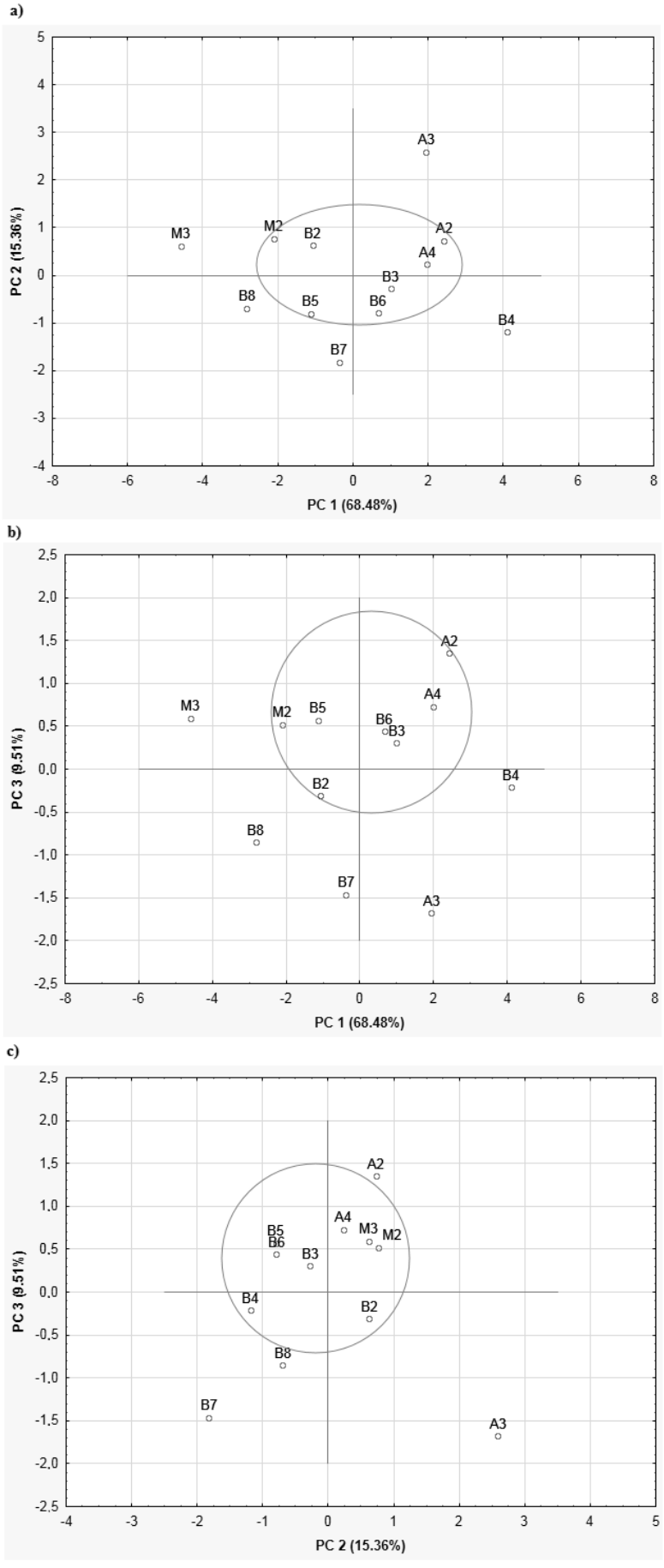
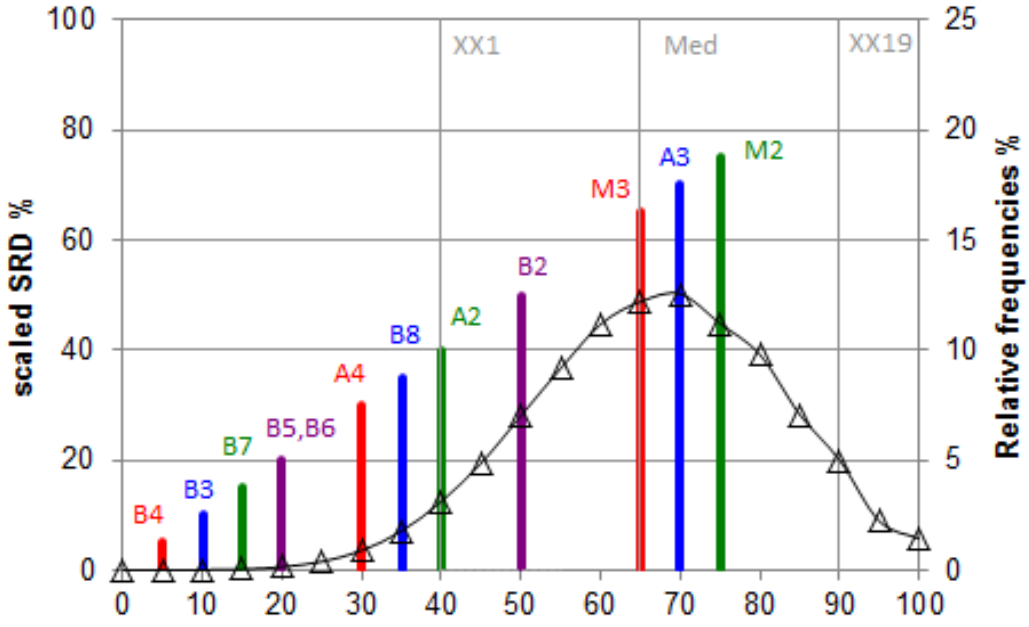

a)
PC 2 (15.36%)
PC 1 (68.48%)
A3
M3
M2
B2
A2
A4
B3
B8
B5
B6
B4
B7
b)
PC 3 (9.51%)
PC 1 (68.48%)
A2
A4
M3
M2
B5
B6
B3
B4
B2
B8
B7
A3
c)
PC 3 (9.51%)
PC 2 (15.36%)
A2
A4
B5
M3
M2
B6
B3
B4
B2
B8
B7
A3

Figure 5


100
80
60
40
20
0
scaled SRD %
25
20
15
10
5
0
Relative frequencies %
XX1
Med
XX19
B4
B3
B7
B5,B6
A4
B8
A2
B2
M3
A3
M2
0
10
20
30
40
50
60
70
80
90
100