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

JOANNA KOŁODZIEJEK,[1] ADAM VOELKEL,[1] KAROLY HEBERGER[2]

[1]Institute of Chemical Technology and Engineering, Poznań University of Technology, Poznań 60-965, Poland

[2]Research Centre for Natural Sciences, Hungarian Academy of Sciences, Budapest H-1025, Hungary

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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. 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^{D}_{S}; K_A and K_D parameters describing the acidity and basicity, respectively; and Flory–Huggins parameter χ'_{23} (the magnitude of interactions). Principal component analysis (PCA) and the procedure based on the sum of ranking differences (SRD) were applied for the 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. © 2013 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 102:1524–1531, 2013

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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 parts 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 such as 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, which 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 toward 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 because of its 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, whereas the siloxane groups are hydrophobic.[7] Biodegradable polymers are frequently

Correspondence to: Joanna Kołodziejek (Telephone: +48-61-6653723; Fax: +48-61-6653649; E-mail: joannakolo@op.pl)

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applied as organic materials because of the fact that products of their metabolic processes are completely removable and nontoxic.[8]

Many experiments including physicochemical tests should be carried out to implement a new hybrid material such as an excipient for 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 the materials used 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 of surface activity by determination of γ^{D}_{S}, the dispersive component of the free surface energy, the acidity and basicity of the surface (K_A and K_D parameters); and Flory–Huggins interaction parameter χ'_{23}, 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 (1) for the measurement of the dispersive component of surface free energy, (ii) for the determination of Flory–Huggins interaction parameters, and (iii) for the determination of solubility parameters in polymer–solvent systems.[12,13]

The aim of this study was the characterization of hybrid materials by IGC and application chemometrics to select one group of materials that could be used as a drug carrier.

Computer programs such as Statistica [StatSoft, Inc. (2005). STATISTICA (data analysis software system), version 7.1. www.statsoft.com.] and Comparision of Ranks by Random Numbers–sum of ranking differences (SRD) allow the assessment of the quality of results including the separation of the parameters most relevant to the studied phenomenon. Experimental data were analyzed by principal component analysis (PCA) and a procedure based on SRD. These methods allow to find 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), and microcellulose was purchased from Rettenmaier (Weibenborn, Germany), which were used as supporting base for hybrid materials. The inorganic part was covered by polymer. The organic constituent of hybrid material was obtained by using one of the following polymers: polyethylene 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 200 mg. Examined materials are presented in Table 1.

IGC Experiments

Inverse gas chromatography measurements were carried out with the use of a gas chromatograph (SMS Ltd.) equipped with a thermal conductivity detector and a flame-ionization detector. Carrier gas was dry helium with flow rate of 15.0 mL/min. Each column was made from glass (internal diameter 4 mm, length 30 cm). The measurements were carried out at 37°C; injector and detector temperature was equal to 150°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 for 2 h at the temperature and flow rate used during IGC experiment. As test solutes, the followings were used:

- nonpolar compounds: hexane (C_6, purity 99%; Chempur, Tarnowskie Góry, Poland), heptane (C_7, purity 99%; Sigma–Aldrich) octane (C_8, purity 99%; Fluka, Poznań, Poland), nonane (C9, purity 99%; Acros Organics, Gliwice, Poland);
- polar compounds: chloroform ($CHCl_3$, analytical grade; POCH S.A., Gliwice, Poland), ethanol (EtOH, purity 99%; POCH S.A.) 1,4-dioxane ($C_4H_8O_2$, purity 99%, Fluka), acetonitrile (CAN, analytical grade; POCH S.A.), and ethyl acetate ($CH_3COOC_2H_5$, HPLC grade; POCH S.A.).

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^{D}_{S} was determined by two methods: Dorris–Gray and Schultz–Lavielle.[14–16] In case of Schultz–Lavielle method, γ^{D}_{S} parameter was calculated based on the following equation:

$$RT \ln V_N = 2Na\sqrt{\gamma^{D}_{S}\gamma^{D}_{L}} + C \quad (1)$$