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Quantitative structure–property relationship prediction of permeability coefficients for some organic compounds through polyethylene membrane

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Abstract

In this work artificial neural network was constructed and trained for the prediction of the permeability coefficients of various organic compounds through low-density polyethylene, based on quantitative structure–property relationship method. The inputs of this network were theoretically derived molecular descriptors which were selected by the stepwise multiple linear regressions technique. These descriptors are; the number of oxygen atoms in a molecule, area-weighted surface charge of hydrogen bonding donor atoms (HA-dependent HDCA-2), molecular transform index lag 11 weighted by atomic van der Waals volume (Morse-11v), molecular transform index lag 10 weighted by atomic polarizability (Morse-10p) and polarity parameter. In order to assess the accuracy and predictability of the proposed model, the cross- validation and Y-scrambling test were employed. The statistical parameters for cross-validation tests are; $R^2 = 0.964$, PRESS = 0.221. The results obtained showed the ability of developed artificial neural network to prediction of permeability coefficients of various compounds. Also result reveals the superiority of the artificial neural network over the multiple linear regressions model.

Keywords: Artificial neural network; Quantitative structure–property relationship; Multiple linear regressions; Permeability coefficient; Molecular descriptor; Polyethylene membrane

1. Introduction

Permeation is the process at which molecules passes through a polymeric membrane. The mechanism of permeation occurs usually by the process (a) sorption and/or solution of the penetrant in the surface of polymer, (b) migration by diffusion of the penetrant molecules to the opposite surface under a concentration (or chemical potential) gradient and (c) desorption and evaporation of the penetrant molecule from the outer surface of polymer. If the desorption and evaporation process are not the rate determining steps, the permeability coefficient (p) can be expressed as the product of the solubility (S) and diffusion (D) coefficient of permeant as follows[1]:

$$p = D \cdot S \tag{1}$$

Penetration of organic compounds in polymers is relevant topics for both theoretical and technological interest. Careful analysis of transport properties could clarify many polymer structural aspects which are influenced by the polymer nature, morphology, density of cross-linking, crystallinity, size of permeate and temperature of propagation among others [2]. The knowledge of permeability is essential for the application of polymer as barrier materials, packages, encapsulations of electronic circuits and in the fields of reverse osmosis, controlled release of drugs and pervaporation process [3]. Since experimental determination of permeability coefficient of various compounds are

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expensive, time consuming and require large amounts of pure sample therefore development of a theoretical method to predict it will be useful and interest. One method is quantitative structure properties relationship (QSPR). QSPR is a mathematical method that relates the properties of interested molecule to its structural features. A current trend in quantitative structure property relationship studies is the use of theoretical molecular descriptors, which can be calculated directly from molecular structure. Obtained QSPR model, can be used to estimate the properties of other molecules even when their structure is only sketchy. There are many reports about the applications of QSPR in chemistry [4–6]. Janzhong and co workers developed a membrane-interaction quantitative structure activity relationship analysis, which was applied on the 18 different membranes [7]. Riviere and Brooks present a hybrid quantitative structure permeation relationship model for prediction of skin permeability of some organic compounds [8]. Chen et al. studied the penetration of a large number of heterogeneous compounds through a polydimethylsiloxane membrane [9]. Recently, Pugh et al. have developed a model for diffusion across human stratum corneum in terms of molecular weight, H-bonding and electronic charge descriptors [10]. Katritzky et al. reported the determination of kinetic chain-transfer constants in polystyrene polymerizations for a set of 90 transfer agents. The descriptors involved in the correlations are well consistent with the proposed mechanism of the chain-transfer reactions [11]. Kholodovych et al. predicted the cellular response to the surfaces of biodegradable polymers by QSPR method. Using the statistic technique partial least squares (PLS) regression, the model was built by fitting experimental data of 62 polyarylates to molecular descriptors, which were based on polymer structure [12]. Reynolds [13] used QSPR technique to predict several polymer properties without extensive experimentation [14,15]. He created virtual polymer library, then employed similarity–diversity analysis and a genetic algorithm-driven QSPR model to design diverse and focused libraries of copolymers. Relationships between the molecular structure of polymer compounds and their glass transition temperatures have been studied extensively [16–20]. Moreover, a detailed description of prediction of glass transition temperature can be found in the recent review [21]. Other quantitative structure–property or structure reactivity relationships (QSAR or QSPR) have been developed for describing gaseous diffusion in polymers [22], modeling transport behavior of amorphous polymeric materials [23], and estimating inelastic mean free paths for polymers and other organic materials [24]. In addition, Gonzalez et al. studied the penetration of 63 compounds through polyethylene by using topological substructural molecular design (TOPS-MODE) methods [25].Today artificial neural network (ANN) was widely used as a nonlinear feature mapping technique in QSPR investigations [26–32]. For example Lim et al. predict the human skin permeability using a combination of molecular orbital calculations and ANN [33]. They used dipole moment, polarizability, sum of charges on nitrogen and oxygen atoms, and sum of charges on hydrogen atoms bonding to nitrogen or oxygen atoms as molecular descriptors. Also, Dem and coworkers predict the skin penetration of selected xenoibiotics by ANN and concluded that ANN modeling was be useful for predicting skin permeability coefficients of organic compounds [34]. The main aim of the present work was to development of a QSPR model using artificial neural network to predict the permeability coefficient of various compounds through low-density polyethylene. In the first step, a multiple linear regression model was constructed, then for inspection of non-linear relation between different parameters in the model, an artificial neural network was generated for the modeling and prediction of the permeability coefficient. By using QSPR method it is possible to interpret the effect of each molecular descriptor to better understanding the types and extent of interaction which occurs during in the permeation of permeant through polymeric membrane.

2. Methodology

2.1. Data set

The permeability coefficients of 63 organic compounds through low-density polyethylene were taken from ref. [2], which was used as data set. This set contains experimental permeability coefficients of different organic compounds such as alkanes, alkenes, alcohols, acids, aromatic compounds and N and O containing organic compounds. The permeability (p) of these compounds are measured as the amounts of permeants (as neat liquid) passing through a polymer film (in g) of unit thickness (in mm), per unit area of membrane (in m^2), per unit of time (in day) which has a unit of g mm/m^2 d. These values obtained under the same conditions. The names of compounds, as well as the calculated and experimental logarithmic values of the permeability coefficient, log(p), of data set are shown in Table 1. Maximum value of log(p) is 2.380 for carbon tetrachloride and the minimum value is −1.553 for benzoic acid. Data set randomly divided into training, test, and prediction sets, each of them containing 43, 10 and 10 members, respectively.

2.2. Molecular descriptors generation

The molecular structures and chemical properties of the polymer and permeant molecule affected on their permeability coefficients. The value of permeability coefficient depends on the steric parameters and the types and extent of various intermolecular interactions, which occurs between permeant and polymeric membrane. Therefore for prediction of the permeability coefficient of organic compounds it is necessary to calculate the molecular structural features of permeant. Due to the diversity of the molecules studied, different descriptors were calculated. These molecular descriptors were mainly computed using the