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Editorial

Michael H. Abraham and His Developed Parameters: Various Applications in Medicine, Chemistry and Biology

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Prof. Michael H. Abraham obtained his B.Sc. degree in chemistry from the Northern Polytechnic London and did his Ph.D. at the University College London and he was a Reader at the University of Surrey, and then became a research fellow at University College London, where he obtained his D.Sc. degree in 1974.[1]

Prof. Abraham's first paper indexed in Scopus backs to 1957[2] and dealt with the chromatographic analysis of peroxides. During 1957-1969 his publications mainly focused on chemistry of organometallic compounds, and in 1969, the first paper dealing with solvent effects on the free energies of the reactants and transition states was published in "Journal of the Chemical Society D: Chemical Communications"[3] when he was working as a Reader at the University of Surrey.

In 1981, Michael published his joint first paper with Prof. Taft (from University of California) and Prof. Kamlet (from a military laboratory in Maryland) dealing with the application of solvatochromic parameters in heterocyclic decomposition of *tert*-butyl halides.[4] Robert W. Taft was one of the pioneers of linear free energy relationships (LFERs) who separated the substituent's effects into polar, steric and resonance influences.[5] A novel method for obtaining scales of hydrogen-bond acidity (a)[6] and hydrogen-bond basicity (b)[7] of the solvents by the solvatochromic comparison was proposed jointly with Mortimer J. Kamlet in 1976. The general p^* scale of the solvent's polarity based on UV-Vis measurements was suggested in collaboration with Kamlet and Abboud.[8] Michael added the Hildebrand solubility parameter as another solvent descriptor for correlation of all types of solvent effects.[9] Taft and his co-authors including Michael have also realized that the solvatochromic solvent equations could be set up to investigate the effects of the solutes, when the solvent system remained constant.[10] In 1983, they published the first joint paper dealing with the solubility properties of the solutes in polymers and biological media.[11] In 1985, solubilities of a range of nonelectrolytes in blood, plasma, brain, lung, liver, kidney, muscle tissue, and human fat were calculated using the developed descriptors.[12] Toxic properties of the compounds were investigated using the developed descriptors in 1986.[13] In 1990, the applicability of the developed descriptors for representation of the upper respiratory tract irritation of male mice by airborne chemicals was shown.[14]

In 1992, Michael was awarded the first of two Ebert Prizes for his paper titled "Role of hydrogen bonding in general anesthesia".[15] The Ebert Prize was established in 1873 which is the oldest pharmacy award. It is presented by the American Pharmaceutical Association to the authors of a published paper in Journal of Pharmaceutical Sciences describing novel and original findings with high probability of significantly impacting the pharmaceutical sciences.[16] Two years later, the general form of the Abraham solvation model was applied to investigate partitioning of some drugs between blood and brain[17] and also in chromatographic systems.[18] In 1995, skin permeation of molecular solutes was described by Abraham solvation model.[19] In 2001, human intestinal absorption of molecular drugs was represented using the Abraham solvation parameters calculated using ABSOLV program.[20] In 2002, this publication[20] was awarded the second of the two Ebert Prizes that Michael received for his research publications.[16] In 2004, Abraham and Zhao[21] introduced the specific ionic descriptors (J^+ and J^-) for cations and anions which opened a window for application of the solvation parameters for describing human skin permeability,[22] human intestinal absorption,[23] artificial membrane retention factors[24] and brain permeation[25] for the ionized forms of the solute molecules. Abraham model correlations have also been reported for describing solute transfer of ions and ionic species from water into more than 30 different organic solvents and into select binary aqueous-organic cosolvent mixtures.

The Abraham solvation model has been successfully applied to correlating the gas to room temperature ionic liquid (RTIL) partition coefficients of volatile organic compounds into more than 100 different RTILs of varying polarity and hydrogen-bonding character.[26,27] Abraham, Acree and coworkers[28] extended the predictive applicability

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of the basic model by splitting the six equation coefficients into a separate cation and anion contribution, which when summed will yield the respective equation coefficient for the given RTIL. At the writing of this editorial coefficients have been reported for 65 individual cations and 20 individual anions. The published cation and anion coefficients allow one to construct Abraham model predictive equations for 1,300 (65 times 20) different RTILs.

The convulsant/anesthetic activity of 48 compounds has been analyzed using an Abraham solvation equation in 2009 and the results revealed that the predicted convulsant pressure is less than that of anesthetic pressure which is in good agreement with the experimental findings for the compounds studied. The difference between the compound pressure to produce convulsions and anesthesia is quite small for many of the 48 compounds, and so minor structural features can be significant.[29] An earlier study[30] had examined the effect of anesthetic structure on inhalation anesthesia of 148 varied anesthetic agents based upon measured values of the minimum alveolar concentration.

In 2011, Abraham and Acree proposed a new method to extend the applicability of the Abraham solvent parameters for calculating the solubility in water-ethanol mixtures in which each solvent composition possesses a given set of the solvent parameters.[31] The approach was later extended to binary aqueous-methanol[32] and aqueous-isopropyl alcohol[33] mixtures. In his last paper published in Journal of Solution Chemistry, water–solvent partition coefficients of fluorescein at an aqueous pH 3.28 for the solvents octan-1-ol, dichloromethane, trichloromethane, 1,2-dichloroethane, toluene, chlorobenzene and bromobenzene were determined and used to compute its descriptors.[34]

Michael was among the most influencing scientist in solution chemistry and his developed descriptors have been used for mathematical representation of many chemical, pharmaceutical and biological processes. Even though Michael formally retired many years ago, he continued to publish many important papers. Near the time of his death he was collaborating with Professor William Green (of Massachusetts Institute of Technology) looking to further the applicability of his general solvation parameter model by examining group contribution and machine learning methods as a means to predict solute descriptors for additional organic and medicinal compounds.[35] Once calculated the solute descriptors can be used to predict a wide range of different properties using the mathematical correlations published by Professor Abraham and researchers. Several of these correlations have been described above.

It should be noted that the Abraham model solute descriptors are not simply curve-fitting parameters, but rather the descriptors encode valuable chemical information regarding how the given solute molecule interacts with neighboring solvent molecules. Solute descriptors, denoted as E, S, A, B. V and L in Michael's recent publications,[19-35] are defined as follows: E denotes to the solute excess molar refractivity in units of (cm^3 mol^{-1})/10, S measures the solute dipolarity/polarizability, A and B pertain to the overall or total hydrogen-bond acidity and basicity, V refers to the McGowan volume expressed in units of (cm^3 mol^{-1})/100, and L is defined as the logarithm of the solute's gas-to-hexadecane partition coefficient measured at a reference temperature of 298 K. The solute descriptors are described in greater detail elsewhere.[36]

The large solute descriptor,[37] blood to brain partition coefficient[38] and skin permeation[22] databases that Michael constructed over the years continue to be used by other researchers working in the pharmaceutical and chemical industries. For example, Yamamoto and coworkers[39] recently examined the absorption of pharmaceutical compounds on several laboratory material surfaces using the Abraham model solute descriptors. As noted by the authors unwanted absorption onto test tubes and other laboratory surfaces can adversely affect the accurate determination of drug concentrations in solution, and lead to miscalculated absorption, distribution, metabolism, and excretion (ADME) properties. Li[40] later utilized published Abraham model water to organic solvent correlations in searching for suitable extraction vehicles (blood simulating solvents) to use in testing the safety of blood-contacting medical devices. Several methods[31-33, 41-43] have employed Abraham model solute descriptors as input parameters for estimating the solubility of medicinal compounds in organic mono-solvents and binary solvent mixtures. The derived expressions provide the pharmaceutical community with an *in silico* means to estimate solubility in the absence of experimental values.

As an indication of the impact that Michael's work had, he continues to be listed among the top 2 % of scientist based on a study titled "August 2021 data-update for 'Updated science-wide author databases of standardized citation indicators" by Jeroen Baas, Kevin Boyack, and John P.A. Ioannidis.[44] He was also a professional painter and spent considerable time painting in the studio, landscape painting and also setting up the art exhibitions.[45] In Jan 2021 Michael sadly passed away and the researchers of solution chemistry lost one of the most active leaders of the field. This editorial was prepared according to an invitation from the Editor-in-Chief of the Pharmaceutical Sciences as the memorial of the first anniversary of his death.

Author Contributions

The manuscript was written by AJ and WEA and approving the final version for submitting in journal.

Conflict of Interest

The authors report no conflicts of interest.

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