separations

Editorial

Hydrophilic Interaction Chromatography

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Hydrophilic interaction chromatography (HILIC) was first introduced by Alpert in 1990 [1]. He mentioned "When a hydrophilic chromatography column is eluted with a hydrophobic (mostly organic) mobile phase, retention increases with hydrophilicity of solutes. The term hydrophilic-interaction chromatography is proposed for this variant of normal phase chromatography".

In the early years of HILIC, relevant studies were sparse, and analytes were also limited to compounds, such as carbohydrates, oligosaccharides, and peptides. Interest in HILIC grew rapidly after 2003, with the number of publications reaching 500 in 2015 (I conducted a search for the terms 'HILIC' or 'hydrophilic interaction (liquid) chromatography' using PubMed). Since then, relevant studies have been consistently published, demonstrating that researchers remain interested in HILIC.

It is important to select an appropriate stationary phase according to the nature of analytes to be separated in HILIC since many kinds of functional groups, such as bare silica, aminopropyl, triazole, diol, amide, sulfoalkylbetaine, and phosphorylcholine are available as a HILIC stationary phase [2]. In this respect, it is essential to explore the mechanism of retention created by HILIC. A water-rich liquid layer immobilized on the surface of stationary phases is critical for retention in HILIC [3]. The volume of the adsorbed water layer varies across a wide range in the stationary phases commonly used in HILIC separation. Moreover, some interactions such as partition, adsorption, and electrostatic take place in HILIC, which is much more complex than those in a reversed-phase mode. Eight retention models were tested to describe the retention of seven highly popular compounds in HILIC columns [4].

HILIC is used for the analysis of highly hydrophilic compounds. Catecholamines are very hydrophilic and weakly retained in reversed-phase conditions [5–7]. Alsaeedi et al. found that core–shell Z-HILIC had a high efficiency following the rapid separation of three catecholamines within 60 s. The developed method was applied to urinary catecholamines analysis [8]. Adenosine, which is a purine ribonucleoside, was also analyzed by HILIC-MS/MS in blood samples [9].

The characterization of several kinds of nutraceuticals was performed based on HILIC with fluorescence detection. The study focused on the determination of flavanols and related compounds, such as condensed tannins. HILIC offered improved possibilities for oligomers separation depending on size features compared to reversed-phase mode.

It is difficult for positively charged basic compounds to have good peak shapes in a reversed-phase mode. HILIC was evaluated as an alternative to reversed-phase columns for the separation of eight adrenoceptor antagonists [10]. HILIC proved to be a viable solution to problem of the poor peak shape for basic compounds.

An analytical method for fosetyl-Al determination in wheat flour was developed using HILIC-MS/MS [11]. A HILIC column provided both the sufficient retention of fosetyl-Al and removal of the matrix in wheat flour. The determination of acetyl hexapeptide-8 in cosmetics was performed using HILC-PDA detection [12]. HILIC caused the efficient retention of acetyl hexapeptide-8 with less matrix effect.

Two-dimensional LC (2D-LC) is attractive method to improve the performance of LC separation, especially for separation of complex samples.

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High orthogonality is obtained by combining different modes of LC. Based on the use of two orthogonal stationary phases, the separation power of 2D-LC system is greatly enhanced when compared to a conventional one-dimensional separation. Sommella et al. compared hydrophilic interaction liquid chromatography x reversed phase (HILIC x RP) and reversed phase x reversed phase (RP x RP) coupled to mass spectrometry for the analysis of complex peptide samples [13]. Both methods showed that the use of two highly retentive trapping columns as a modulation interface delivers high peak focusing and boosts sensitivity and efficiency. Various 2D-LC methods to characterize water-soluble, synthetically grafted bio-polymers, consisting of long poly(acrylic acid) chains and short maltodextrin grafts were evaluated [14], and the combination of HILIC x RPLC proved most informative.

Finally, *Separations* has a Special Issue, entitled "Advances in Hydrophilic Interaction Chromatography" (Guest Editors: Prof. Dr. Alessia Ciogli and Dr. Giulia Mazzoccanti) which will be of great interest for readers who wish to learn more about the latest advances in HILIC. In the future, it is hoped that HILIC becomes a more valuable tool for the separation analysis of polar compounds.

Conflicts of Interest: The authors declare no conflict of interest.

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