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A Short Note on Applications of Mixed Mode Chromatography in Pharmaceutics

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DESCRIPTION

Mixed Mode Chromatography (MMC) is becoming increasingly popular in pharmaceutical and biopharmaceutical applications due to its unique selectivity and retention of a wide range of compounds, especially polar and charged molecules. It is a chromatographic technique in which solutes interact with a stationary phase through multiple interaction modes or mechanisms. MMC has been used as an alternative or complementary tool to traditional reversed-phase, ion-exchange, and normal-phase chromatography. In contrast to RP, NP, and IEX chromatography, where hydrophobic, hydrophilic, and ionic interactions are the dominant modes of interaction, respectively, mixed-mode chromatography uses these modes of interaction.

Mixed-mode phenomena have historically been regarded as second-order interactions. Most stationary phases are based on rigid support matrices such as silica gels or polymers to which specific functional groups are attached. Solutes often interact with matrices and functional groups in a variety of ways, producing secondary interaction properties. Mixed-mode IEX and RP interactions can also be observed on conventional silica-based RP columns without the intentional introduction of ion exchangers. Free silanol groups on silica matrices are considered sites for secondary interactions in RP chromatography. Similarly, hydrophobic interactions exist in IEX separations and ionic interactions exist in SEC separations. In some cases secondary interactions are considered beneficial for selectivity, but in most cases they are considered detrimental to the separation. For example, free silanol groups on silica often contribute to peak tailing. This phenomenon is minimized by end capping or optimizing mobile phase conditions. Mixed Mode Chromatography (MMC) can retain and separate small polar drugs and related substances that are not retained by regular RP-HPLC. It has been used as an alternative to conventional ion chromatography for counterion analysis. MMC has been used to purify biological samples and allows for direct sample injection. Mixed Mode Chromatography (MMC) can retain acidic and basic compounds under mild mobile phase conditions compatible with MS detection. The dominant separation mechanism for a particular mixed-mode column depends on sample properties and mobile phase conditions. Recently introduced mixed-mode stationary phases achieve desirable and reproducible secondary interaction or tertiary interactions by using carefully designed functional groups with different retention modes and well-controlled manufacturing processes provide interaction. The recent commercialization of mixed-mode columns has greatly enhanced the usefulness of MMC in pharmaceutical and biopharmaceutical applications.

Mixed-mode columns are also used in two-dimensional liquid chromatography, as MMC complements RP and other separation modes. Additionally, multimode retention mechanisms can add dimension to a single mixed-mode column by adjusting mobile phase conditions. In addition to silica-based mixed-mode columns, polymer-based mixed-mode HPLC columns are also available. Anion-exchange selectivity is provided by an anion-exchange micro-bead latex that coats the outer layer of the hydrophobic core. Due to the complexity and diversity of analytes in terms of hydrophilicity and ionization, it is difficult, but desirable, to separate anions, cations, and neutral molecules in a single HPLC run. Mixed Mode Chromatography (MMC) offers unique selectivity, especially for polar and charged analytes. Multiple interaction mechanisms allow users to customize mobile phase/eluent conditions to promote specific interactions for specific analytes. MMC has been successfully used in pharmacy for counter ion analysis, polar and charged APIs, impurities, pharmaceutical excipients, environmental and biological samples.

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CONFLICT OF INTEREST

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