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## Solvent Effects in Liquid Chromatography: Peak Anomalies and Solutions

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The solvent effect in liquid chromatography refers to the phenomenon where the interaction between the sample and the mobile phase leads to abnormal chromatographic behavior. Traditionally, solvent effects are commonly understood as the peak distortion caused by the higher solubility of the sample in the liquid phase compared to the pure sample. For example, when a sample is dissolved in 100 % pure acetonitrile and injected into a reversed-phase chromatography system with acetonitrile-water (18:82) as the liquid phase, peak splitting or tailing may be observed.

However, this traditional understanding cannot fully explain other peak distortion phenomena caused by the choice of the mobile phase. For instance, when a sample is extracted in a pH 6.8 dissolution medium and then injected into certain buffer-salt systems, unstable retention times and peak deformations may occur.

To comprehensively understand and explain these phenomena, we need to expand the concept of solvent effects. The following expansions are as follows:

1. Differences in elution strength: This is the solvent effect commonly understood, referring to the differences in retention behavior between the sample and the liquid phase.
2. Differences in ionization state: Some active pharmaceutical ingredients have ionizable characteristics, such as salicylic acid, paracetamol, and paroxetine sodium. These samples exist in both ionized and non-ionized states, with different distribution coefficients between the liquid and stationary phases. In reversed-phase systems, the non-ionized state is more likely to interact with the stationary phase, resulting in longer retention times, while the ionized state has a stronger interaction with the liquid phase, leading to weaker retention. If there is a significant difference between the ionization state of the sample and the liquid phase, unstable retention times and peak deformations may occur. To address this issue, one can dilute the sample solution with the liquid phase, reduce the injection volume, or increase the buffering capacity of the liquid phase.
3. Differences in solubility: In comparative tests using reference standards' dissolution curves, surfactants are often used in the dissolution medium. At times, this may lead to unstable retention times for the sample. This is also due to significant differences in the distribution coefficients of the sample between the diluent and the stationary phase compared to the liquid phase. To address this, one can add the same surfactant to the liquid phase or adjust the ratio of the diluent and the liquid phase.

The understanding of solvent effects can be expanded to include abnormal chromatographic behavior resulting from differences in certain components in the sample between the diluent and the liquid phase. To address such issues, one can employ methods such as diluting the sample solution with the liquid phase, reducing the injection volume, or increasing the buffering capacity of the liquid phase. While there may be other differences in liquid chromatography, they are not discussed here due to space limitations. In conclusion, you can refer to the aforementioned situations for explanation and solution.

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