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The structure of solutions of active pharmaceutical ingredients: the case study of sulfonamides compounds

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One of the oldest methods used by man to obtain solid materials is crystallization from solution. However, to this day, limited information exists on how molecules aggregate in a solution to create a crystal, which limits the ability to control this process. As a result, the same molecule often precipitates with different crystal packings, leading to materials with significantly different physical properties (e.g., solubility and bioavailability). This phenomenon known as polymorphism, is critical for the pharmaceutical industry, where the produced materials need to maintain their properties throughout the manufacturing process.[1]

The crystallization control problem can be traced, in part, to the lack of information on the structural transformations occurring in the solution during the nucleation process. Thus, comprehensive knowledge about the molecular aggregation (solution structure) is required if tight control over a crystallization process is in view. In this work, the structure of methanol and acetonitrile solutions of the active pharmaceutical ingredients of the sulfonamide family of compounds (Figure 1) was investigated based on (*i*) the determination of temperature versus concentration phase diagrams, (*ii*) nuclear magnetic resonance studies, and (*iii*) differential scanning calorimetry methods. These studies revealed, so far, that the aggregation of solute molecules begins before saturation of solution is achieved during a cooling crystallization procedure, a finding that contradicts the current nucleation theories. Finally, the crystallization pathway seems to be influenced by the solvent and the solution concentration, suggesting that these factors can be used to control the outcome (crystal phase) of the crystallization process of the sulfonamide compounds.

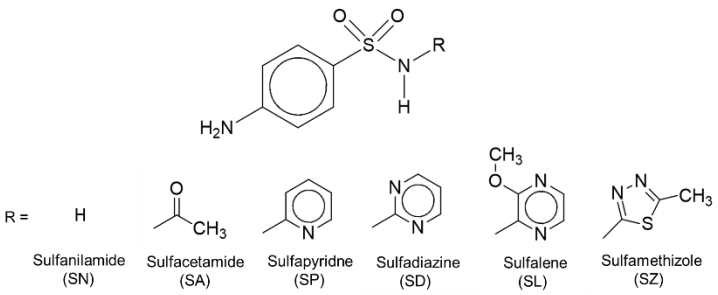

Figure 1. Active pharmaceutical ingredients investigated in this work.

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References

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