

### Quartz Crystal Microbalance Technique for Analysis of Crystallization: Analysis of Solubility, Supersaturation, Nucleation and Phase Transformation

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In the present study a new QCM technique is addressed regarding to determinations of the solubility, induction of nucleation, supersaturation and phase transformation in cooling crystallization of sulfamerazine. When cooling a solution, a sudden refraction of the resonant frequency and resistance of the QCM responses occurred at the point of the first primary nucleation due to a formation of solid mass on the QCM sensor, representing the induction point. Inversely when heating the suspension, a significant profile change of resonant frequency and resistance was similarly observed at the saturated point due to the complete dissolution of solid crystals, representing the solubility. When the sensor surface was modified with  $-NH_2$ , it prevented the crystal formation of metastable form (Form-I) on the sensor surface, allowing the sensor to detect the property change only in the solution phase. Thus, the resonant frequency shift reflected only the supersaturation change during the cooling crystallization of sulfamerazine. Also the phase transformation to stable form (Form-II) was detectable because the stable crystals could be formed on the  $-NH_2$  modified surface.