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Equilibrium solubility measurements of two carvedilol polymorphs with saturation shake-flask method and with real-time monitoring

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The study of polymorphism is important in drug research and development, since the different physico-chemical properties of the polymorphs may affect the stability, solubility, dissolution, and therefore the bioavailability of the substance. In our work, we investigated the pH-dependent equilibrium solubility of two carvedilol polymorphs according to a standard protocol, in the pH range of 3-11, using saturation shake-flask method and µDISS device. Measurements were performed using two solutions: Britton-Robinson (B-R) with standard ionic strength, and B-R buffer where the ionic strength was modified with 0.15 M KCl. Solubility results were compared to the values predicted by the Henderson-Hasselbalch equation. In two different buffers (pH 6 and 6.5), in-situ UV probes were used to monitor the dissolution in real-time, so it was possible to obtain precise information on the time needed to achieve the equilibrium, and the rate of supersaturation. At the end of the solubility measurements, the solid phase analysis of the samples was performed by X-ray powder diffraction and Raman spectroscopy. Twofold difference was found between the solubility of the two forms. It was proved that the crystalline structure of the two polymorphs does not change during the measurement, and salt formation could be observed in the acidic pH range (pH≤6.5). The counterion and solubility of the salt were found different in various buffer solutions.

Biography

Dóra Csicsák is a second year PhD student in the Department of Pharmaceutical Chemistry at Semmelweis University, Hungary. She graduated from Semmelweis University's Faculty of Pharmacy in 2017. In her doctoral research, she investigates the dissolution and permeabilty of polymorphous, amorphous, micro- and nanosized drugs.

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