Impact of polymer strength on precipitation kinetics of acidic drugs

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Supersaturated solutions are metastable forms of the drug. The metastability is attributed to the intrinsic thermodynamic instability of the systems. Where higher chemical potential leads to the increased permeability and bioavailability of the drug molecules in the systems, the same ‘escaping tendency’ of solute leads to the precipitation of the drugs thereby, leading to loss of the solubility advantage. Hence, in order to optimize bioavailability from the supersaturated drug delivery systems (SDDS), it becomes important to quantify the time-dependent solubility advantage as well as the stability of the supersaturated systems. In the current study, atorvastatin calcium (ATC), a poorly soluble weakly acidic drug was used as a model drug for understanding the impact of polymer strength in maintaining the degree of supersaturation over time. Polymers Eudragit EPO and polyvinyl pyrrolidone K30 were used at different concentrations vis. 0.02, 0.05, 0.1 and 0.5 (w/v %) with the supersaturation being generated by solvent shift method. UV spectrophotometry was used to monitor the change in concentration over time. As a practical substitute of nucleation time, the time taken for decrease in concentration by 1% i.e. t1% was selected as we were able to quantitatively distinguish the initial precipitation behaviour of drug in the presence of polymers at this time. Below t1%, a lot of variability was observed, whereas above this value, crystal growth rate might predominate. Since we know that nucleation usually starts followed by crystal growth, a simple method was adopted to distinguish the effect of polymers on ATC precipitation. In our study, t10% provides information about the crystal growth. The smaller the time difference (Δt) from t1% to t10%, the faster is the crystal growth rate. Any effect on t1% would signify the effect on the nucleation step, while changes in Δt = (t10%-t1%) would signify the effect on crystal growth. In precipitation studies, spontaneous nucleation and crystal growth were observed for ATC when no polymer was added. This indicates that the supersaturated solution was in an unstable labile zone. The degree of supersaturation involved in the system was high, so the poorly soluble drug in solution precipitated out rapidly. In the absence of polymers, once the nucleation is initiated at these high supersaturation levels, the crystal growth rate of ATC was high. However, in the presence of Eudragit EPO, the onset of nucleation was delayed, while the crystal growth rate was unaffected as represented by Δt. The precipitates so obtained were characterized via powder XRD, DSC, FT-IR and SEM to understand any change in solid state properties or drug-polymer interactions. The results so obtained are targeted to be applied in designing formulations within the absorption window of the drugs.


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