A quantitative approach to monitoring antisolvent crystallization of clopidogrel hydrogen sulphate by Raman spectroscopy

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Polymorphism is the ability of a compound to crystallize as more than one distinct crystal species. Properties of APIs such as bioavailability, compressibility, dissolution, stability and shelf life are affected by form of the polymorph.
In this study, quantification of form I and form Ⅱ of clopidogrel hydrogen sulphate (CHS) was monitored. Antisolvent crystallization of CHS was carried in a methanol-isopropanol mixture while been monitored by Raman spectroscopy in-line. Experiments were conducted at 25 oC using an antisolvent fraction of 0.7 to 0.85. The induction times of form I and Ⅱ were easily deduced which is critical to the kinetics of the system. Validated partial least squares method was successfully used in the quantification of form Ⅱ in the polymorph mixture.