Production of amorphous submicron particle and design of solid dispersion formulation of sulfasalazine using supercritical antisolvent process

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Particle design of poorly water-soluble active pharmaceutical ingredient (API) such as the microparticle production, amorphous particle generation and solid dispersion formulation is the strategy to enhance the dissolution profile and bioavailability. Supercritical fluid technology is an intensified process to efficiently manipulate the solid-state property of API and have been used in formulation design in literature. In this study, supercritical antisolvent (SAS) process was used to produce amorphous submicron particle and design polymeric amorphous solid dispersion of sulfasalazine for the purpose of dissolution improvement. Sulfasalazine is a poorly water-soluble API, which is used to treat rheumatoid arthritis, ulcerative colitis, and Crohn'sdisease. Supercritical carbon dioxide was used as an anti-solvent in this SAS study. Analytical instruments such as SEM, DSC, PXRD, FTIR, and TGA were used to compare and discuss the modification of the solid-state properties of drug powders before and after SAS process. Regarding the amorphous submicron particle production, according to the solvent screening experiments, an appropriate cosolvent system was decided and amorphous submicron particle of sulfasalazine was generated successfully. The operating parameters of SAS were further explored and found operating at a high carbon dioxide flow rate, low operating temperature, and smaller nozzle diameter favor the production of small drug particle, while the effect of operating pressure and solution concentration are relatively insignificant. At the optimizing condition, submicron amorphous powder with mean size of 0.36 μm was obtained through SAS. In addition to SAS study of API processing, this study also designed and prepared the polymeric amorphous solid dispersion formulation of sulfasalazine. PVP (Polyvinylpyrrolidone) was selected as the polymeric carrier. The effect of cosolvent ratio, drug/polymer ratio, temperature, pressure, carbon dioxide flow rate, and solution flow rate in SAS were investigated. In terms of the mean particle size, the effects of the solution flow rate and the nozzle diameter are the most significant operating parameter. In this study, the polymeric amorphous solid dispersion powder with mean size of 0.47 μm were generated with satisfactory recovery yield up to 90%. Finally, the dissolution study was conducted and the dissolution of sulfasalazine from solid dispersion formulation prepared by SAS is significantly improved compared with the physical mixture sample. These results demonstrate SAS is an efficient technique in both submicron particle production and formulation design in pharmaceutical application.