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Process Control and in Vitro/in Vivo Evaluation of Aripiprazole

Sustained-release Microcrystal for Intramuscular Injection

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Abstract: This work describes the preparation of aripiprazole sustained-release microcrystals for intramuscular injection, through recrystallization, drying, wet grinding and solidification steps, which all had a great impact on product quality. Here, we evaluated the crystal form of the drug in each step by differential scanning calorimetry (DSC), powder x-ray diffraction (PXRD), and fourier transform infrared spectroscopy (FT-IR), demonstrating that there is no change in the crystal form of aripiprazole monohydrate (H1) during grinding and freeze-drying. Microscopy and scanning electron microscope (SEM) data showed that freeze drying had no effect on the morphology of milled-H1, and thermal gravimetric analysis (TGA) results showed that the freeze-dried formulation was acceptable for water content. In particular, in this study, a similarity factor fitting was applied for the similarity of the particle size cumulative distribution curve, and the similarity factor value (99.00) showed that there was no change in the particle size distribution before and after freeze-drying. A two-chamber transmembrane method was used to investigate the in vitro release of the aripiprazole sustained-release microcrystal (ALSI) and commercial preparations (Abilify Maintena®). The similarity factor fitting of in vitro release profiles and drug cumulative release curves in vivo yielded similarity factor values of 98.00 & 95.43, indicating similar in vitro release and in vivo bioavailability of rats between the ALSI and Abilify Maintena®. A single-dose administration could produce long-term effects for a month. For the microcrystalline suspension, in addition to the conventional quality control indicators, the similarity of the cumulative particle size distribution, the in vitro release profile, and the similarity of the drug release percentage in vivo can be used to reflect product quality and process control.

Keywords

Aripiprazole Monohydrate; Sustained-release Microcrystalline; Freeze-drying; Similarity

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