MS28-1-8 New multicomponent crystals as a method to improve the physicochemical properties of active pharmaceutical ingredients – three case studies
#MS28-1-8

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Abstract
Multicomponent pharmaceutical crystals, consisting of cocrystals and salts, have found use as an alternative solid form of drugs with better physicochemical properties compared to the corresponding parent drugs. The purpose of creating multicomponent crystals is to improve the solubility profiles and dissolution rate of drug molecules, but also to help overcome other problems such as hygroscopicity, poor tabletting, instability, and bitter taste. We aimed to obtain new salts of memantine (MEM) with reduced hygroscopicity and improved taste compared to currently used memantine hydrochloride, which is slightly hygroscopic and has a bitter taste. Another goal was to improve the solubility and release profile of two poorly soluble drugs: febuxostat (FEB) and erlotinib (ETB) by creating new multicomponent systems.
The synthesis was performed by reacting MEM free base with sweet-tasting acids: acesulfame, saccharin, and anthranilic acid. In a case of FEB and ETB, the liquid assisted milling method has been used successfully to obtain new multicomponent crystals. Fourier transformed infrared spectroscopy and powder X-ray diffraction were used to provide information about the formation of new substances. The crystal structure of the new obtained crystals was determined by single crystal X-ray studies. Structural studies were supported by solubility and dissolution rate tests. In the case of MEM, also taste tests.
Each of new MEM salts has an improved taste and is less hygroscopic than memantine hydrochloride. Solubility and dissolution research show that newly obtained multicomponent crystals of FEB and ETB exhibit almost three times higher solubility and dissolution rate than their free bases.
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Crystal structures of memantine salts.