

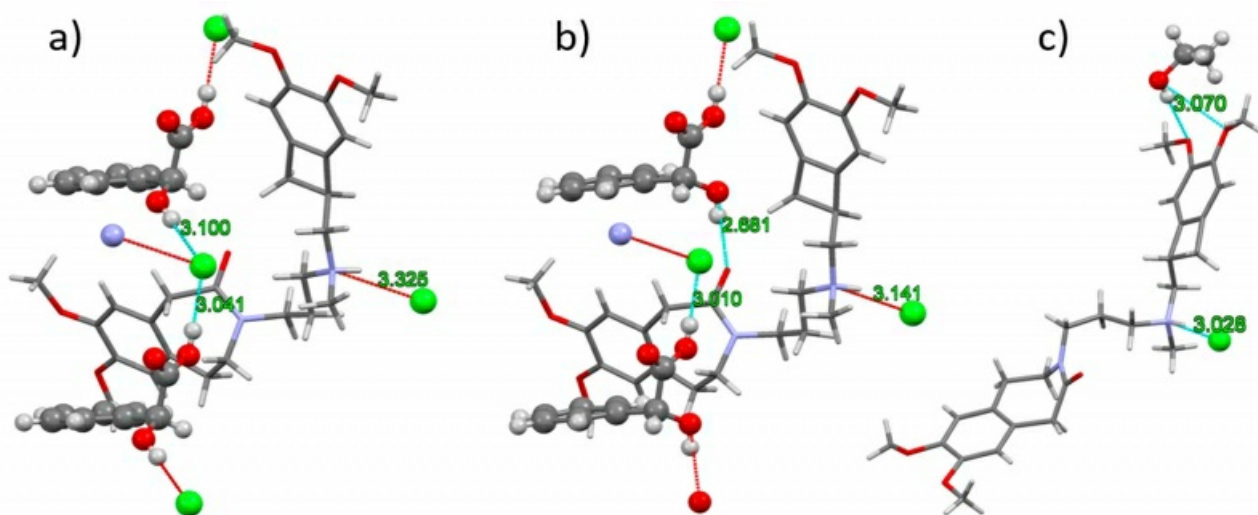
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*Ivabradine hydrochloride mandelic acid cocrystals: two peas in a pod*Veronika Sládková¹, Ondrej Dammer², Eliska Skorepova¹, Bohumil Kratochvíl¹¹University Of Chemistry And Technology Prague, Prague 6, Czech Republic, ²Zentiva k.s., Prague, Czech Republic
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A pharmaceutical salt ivabradine hydrochloride (IVA HCl) is indicated for the symptomatic treatment of chronic stable angina pectoris and a chronic heart failure. It exhibits extensive polymorphism and cocrystallization could be a way to provide an alternative solid form. We performed a cocrystal screen, from which two hits were identified: ivabradine hydrochloride (S)-mandelic acid 1:1 (ICISM) and ivabradine hydrochloride (R)-mandelic acid 1:1 (ICIRM). Both structures were successfully determined from single crystal X-ray diffraction data as cocrystals. The cocrystals were further characterized by common solid state techniques, such as X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), solid state NMR, IR and Raman spectroscopy, and dynamic vapor sorption (DVS). [1]

To decide which of the newly prepared cocrystals was more stable and which could be thus selected for further development, the maturation experiments were designed. We let IVA HCl mature in various solvents in slurries with twice the excess of racemic mandelic acid, with the intention of crystallizing enantiomerically pure, preferred cocrystal. The resulting solids were mixtures of the cocrystals and were measured by XRPD both on flat Si holder and in a capillary (Bragg-Brentano and Debye-Scherrer configurations) and the phase quantification of the powder patterns was done by Rietveld refinement in Jana2006 and HighScore Plus software. However, the similarity of the two structures of ICISM and ICIRM (similar unit cell parameters and overall crystal packing) resulted in the algorithm getting confused during the refinement. The limits of the Rietveld fit in this example are discussed.

[1] Sládková, Veronika, et al. "Ivabradine Hydrochloride (S)-Mandelic Acid Co-Crystal: In Situ Preparation during Formulation." *Crystals* 7.1 (2017): 13.



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