DIKETO-KETOENOL TAUTOMERS IN CURCUMINOIDS

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Curcumin represents a class of natural drugs possessing wide range of pharmacological properties including anti-inflammatory and anti-oxidant activities.[1,2] Curcumin and its derivatives exist in an equilibrium between diketo and ketoenol tautomers. Each of the tautomeric states exhibits dissimilar potency to bind biomacromolecules which affects their pharmacological activities.[3]

In this work, we present comprehensive NMR studies of curcumin analogues in different solvents. We described equilibrium properties of curcumin and its 12 derivatives including pharmaceutical ingredient ASC-JM17 (1, Figure 1) in different solvents. Moreover, we separated two tautomers of ASC-JM17 on column chromatography and studied their equilibration in solution. Solid-state NMR and X-ray diffraction studies revealed two new polymorphs of ketoenol tautomer of ASC-JM17 (1KE, Figure 1).

Figure 1. A) The keto-enol equilibrium of compound 1 and the time-dependence of relative concentration, $c_{rel}$ of 1KK and 1KE obtained from $^1$H NMR spectra after dissolution of the pure KE form. The OH, H4 and methoxy-group region of $^1$H NMR spectra of B) lyophilizate containing over 95 % of the KK, C) the crystalline 1KE and D) the equilibrium mixture in $d_6$-DMSO at room temperature. Note that the first NMR experiment, $t = 0$, was recorded about 3 minutes after dissolution of the compounds.

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REFERENCES