Study of polymorphs and solvates/hydrates of DHEA

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5. SUMMARY

The main goal of the work was to study about polymorphism in the compound dehydroepiandrosterone (DHEA). Special attention was given on the characterization, thermal stabilities, and energetics of the polymorphic forms.

In the work performed, we managed to prepare and characterize the anhydrous, solvate/hydrate forms of our compound through screening test and X-ray powder diffraction. Various new mixture of forms like FI+FII, S2+S5 and FI+S2 were identified which were never observed in the literature.

Apart from this, TG analysis was also used to characterize different forms and also to compute stoichiometries of the different solvates/hydrates. Weight losses of different solvates/hydrates were observed, and the values recorded were seen in a good agreement with the values given in the literature. On the other hand, we also concluded that the morphology of the crystals had an effect on the stability of different forms, as seen for monohydrate S2 obtained from different solvents.

Further, as we already know that an API should be stable for drug formulation. So, to determine the stability of the obtained solvates/ hydrates, TG and X-ray analysis was performed again after 2-3 weeks. In general, which led to the conclusion that with time, forms started to lose mass at lower temperatures and also decomposed fast. On the other hand, from X-ray analysis we concluded that, crystallinity of the forms started decreasing and they started to become amorphous with time. This sort of stability analysis with time was not seen in the literature. On the other hand, during the analysis we also identified a new solvate of methanol for this compound and which needs to be investigated in the future based on the single crystal data.

The energetics part allowed us to determine the melting temperature of the anhydrous forms by using DSC experiments. The enthalpy of fusion of 23.9 ±0.6 kJ mol^{-1} and enthalpy of sublimation of 136.6 kJ mol^{-1} was also calculated for the most stable form i.e., FI. Moreover, a phase transition was also observed for DHEA around 370 K which was never observed in the literature. Not only the transition was observed, but we also identified that this transition is FII converting to FI.