Investigations into the polymorphic forms of Active Pharmaceutical Ingredients (APIs) are of vital importance to drug formulations and are often kept a closely guarded secret by pharmaceutical companies. This secrecy is maintained as the nature of the polymorph could either make or break a drug formulation. Polymorphism is the ability of a solid crystalline form to exist in more than one structural arrangement. The variation in the crystalline forms often displays different mechanical, thermal, and chemical properties. These changes can remarkably influence the bioavailability, hygroscopicity, stability and other performance characteristics of the API [1]. Isoniazid, a well-known pharmaceutical, is used as a first-line treatment against Mycobacterium tuberculosis (TB) which is known to possess multiple polymorphs. Derivatives of isoniazid were developed in response to TB drug resistance. One such derivative, isonicotinic acid-(1-phenyl-ethylidenehydrazide) (IPH) [2] was found to exhibit an array of polymorphic behaviour as a result of its hydrogen bond acceptors, donors and conformational freedom along its backbone. To date only one crystal structure of IPH has been reported in the literature [3]. We have discovered and isolated an additional five novel polymorphs of IPH from various crystallization techniques, namely slow cooling, rapid evaporation, sublimation, as well as from hot-stage experiments. All of the polymorphs display hydrogen bonding through the carbonyl acceptor and hydrazide donor. However the torsion of these hydrogen bond acceptors and donors, relative to the molecular backbone, deviate due to the conformational flexibility of the molecule. Structural information of the polymorphs was obtained by SCXRD, PXRD, IR and Raman. The thermal phase relationships of these polymorphs were also investigated using DSC and HSM. Elucidating these novel polymorphs and establishing phase relationships are a key step in the design of isoniazid based pharmaceuticals.


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