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Water and stability of pharmaceutical solids

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Solid pharmaceuticals are multi-component systems consisting of an active pharmaceutical ingredient (API) and inactive ingredients (excipients). Excipients may include inorganic salts (e.g., NaCl), carbohydrates (e.g., lactose), and polymers, to name a few, whereas APIs range from relatively simple molecules (e.g., aspirin) to proteins and olygonucleotides. Pharmaceutical solids could exist either as single-phase or heterophase systems. They also may have different extent of order, such as highly ordered crystalline phases, amorphous solids that are thermodynamically unstable but might be kinetically stable under the time frame of observation, and crystalline mesophases including liquid crystals. With all this diversity, there are common features for such systems, and two of them will be discussed in the presentation. (i) Requirements for chemical stability of pharmaceuticals are very strict. A very limited (e.g., less than 0.1%) extent of conversion is allowed in these materials over the shelf life, i.e., during several years of storage at ambient and (sometimes) not fully controlled (e.g., a medicine cabinet in one's bathroom) conditions. (ii) All pharmaceutical solids contain some water, although its amount and physical state are highly variable and may change during manufacturing and shelf life. There are many challenging questions and issues associated with the "Water and stability of pharmaceutical solids" subject; some of them will be considered in the presentation: (i) What are the features of chemical reactivity of crystalline vs disordered systems? (ii) What is the role of water in solid state chemical reactivity of amorphous solids, e.g., water as plasticizer vs reactant vs reaction media? (iii) How homogeneous are pharmaceutical amorphous solid solutions, e.g., carbohydrate-water systems? (iv) What is the optimal water content? With water being the most common destabilizing factor, is "the drier - the better" always the case?