

## **Influence of processing conditions on dehydration kinetics - use of non-ambient XRD to monitor *in situ* phase transformations.**

Thakral, S\* and Garcia-Barriocanal, J

Characterization Facility, College of Science and Engineering, University of Minnesota, 55455.

\*Presenting author

**Introduction.** The manufacture of pharmaceutical dosage forms entails numerous unit operations, which can cause change in the physical form of active pharmaceutical ingredient (API). The process of wet granulation can induce formation of API hydrate/s or their mixture. When subsequently dried, a higher hydrate may convert to lower hydrate/s or may dehydrate only partially, eventually leading to presence of mixtures of API forms in the final formulation. The dehydration can be further complicated due to presence of excipients, such as diluent, binder, glidant, in the granule blend. Use of non-ambient stage in an X-ray diffractometer facilitates direct monitoring of solid-state transformation of API physical forms during drying.

**Method.** Sodium naproxen, the model drug, was exposed to varying water vapor pressures to obtain mono, di and tetrahydrate. The drying was simulated under number of conditions to follow the dehydration kinetics of sodium naproxen hydrates. Isothermal dehydration, with simultaneous XRD data collection, was conducted under (i) ambient atmosphere, (ii) controlled flow of inert gas, (iii) low pressure, (iv) high pressure environment and (v) in shear cell. Similar studies in presence of poly (vinyl pyrrolidone), a commonly used binder, are proposed.

**Results.** Slight heating of sodium naproxen dihydrate led to formation of monohydrate, which could only be dehydrated further, either by heating to higher temperature ( $\geq 60$  °C) or under vacuum (at 25 °C). Tetrahydrate form was stable only at higher relative humidity and readily converted to lower hydrate when exposed to water vapor pressure  $\leq 75$  % at 25 °C. Further studies in presence of binder such as PVP, are currently in progress.

**Conclusion.** By modulating sample stage assembly of XRD sample holder, it is possible to simulate pharmaceutical unit operation and monitor *in situ* phase transformations of API. Such studies are of fundamental importance in preformulation phase, as physical form of API can influence the manufacture and performance of the final dosage form.