Chadha, R. and S. Bhandari (2014). "Drug-excipient compatibility screening—Role of thermoanalytical and spectroscopic techniques." *J Pharm Biomed Anal* 87:82–97.

Estimation of drug-excipient interactions is a crucial step in preformulation studies of drug development to achieve consistent stability, bioavailability and manufacturability of solid dosage forms. The advent of thermoanalytical and spectroscopic methods like DSC, isothermal microcalorimetry, HSM, SEM, FT-IR, solid-state NMR, and PXRD into preformulation studies have contributed significantly to early prediction, monitoring and characterization of the active pharmaceutical ingredient incompatibility with pharmaceutical excipients to avoid expensive material wastage and considerably reduce the time required to arrive at an appropriate formulation. Concomitant use of several thermal and spectroscopic techniques allows an in-depth understanding of physical or chemical drug-excipient interactions and aids in selection of the most appropriate excipients in dosage form design. The present review focuses on the techniques for compatibility screening of active pharmaceutical ingredient with their potential merits and demerits. Further, the review highlights the applicability of these techniques using specific drug-excipient compatibility case studies.

Dutta, A. K. et al. (2011). "Physicochemical characterization of NPC 1161C, a novel antimalarial 8-aminoquinoline, in solution and solid state." *AAPS Pharm Sci Tech* 12(1):177–191.

NPC 1161C is a novel antimalarial drug of interest because of its superior curative and prophylactic activity, and favorable toxicity profile against in vivo and in vitro models of malaria, pneumocystis carinii pneumonia, and leishmaniasis. The preformulation studies performed included determination of pK(a)s, aqueous and pH solubility, cosolvent solubility, log P, pH stability, thermal analysis, and preliminary hygroscopicity studies. The mean pK(a1), pK(a2), and pK(a3) were determined to be 10.12, 4.07, and 1.88, respectively. The aqueous solubility was found to be 2.4 × 10(−4) M having a saturated solution pH of 4.3–5.0 and a low intrinsic solubility of 1.6 × 10(−6) M. A mathematical model of the pH-solubility profile was derived from pH 2.2 to 8.0. An exponential decrease in solubility was observed with increasing pH. The excess solid phase in equilibrium with the solution in aqueous buffers was determined to be the free-base form of the drug. A significant increase in solubility was observed with all the cosolvents studied, in both unbuffered and buffered systems. Mean log P of the salt and the free base were estimated to be 2.18 and 3.70, respectively. The compound had poor stability at pH 7.0 at 37°C, with a t (90) of 3.58 days. Thermal analysis of the drug using DSC and TGA revealed that the drug is present as a semi-crystalline powder, which transformed into the amorphous state after melting. The drug was also found to sublime at higher temperatures. Determination of physicochemical properties of NPC 1161C provided useful information for the development of a dosage form and preclinical evaluation.

Erxleben, A. (2016). "Application of vibrational spectroscopy to study solid-state transformations of pharmaceuticals." *Curr Pharm Des* 22(32):4883–4911.

Understanding the properties, stability and transformations of the solid-state forms of an active pharmaceutical ingredient (API) in the development pipeline is of crucial importance for process-development, formulation development and FDA approval.