be assessed and how they are implicated in both discovery enablement and in final product developability of the selected candidate.

Hofmann, M. and H. Gieseler (2018). "Predictive screening tools used in high-concentration protein formulation development." *J Pharm Sci* 107(3):772–777.

This review examines the use of predictive screening approaches in high-concentration protein formulation development. In addition to the normal challenges associated with protein formulation development, for high-concentration formulations, solubility, viscosity, and physical protein degradation play major roles. To overcome these challenges, multiple formulation conditions need to be evaluated such that it is desirable to have predictive but also low-volume and high-throughput methods in order to identify optimal formulation conditions very early in development without time- and material-consuming setups. Many screening techniques have been reported for use in high-concentration formulation development, but not all fulfill the requirements mentioned previously. This review summarizes the advantages and disadvantages of different screening approaches currently used in formulation development and the correlation of predictive data to protein solubility, viscosity, and stability at high protein concentrations.

Kawakami, K. (2012). "Modification of physicochemical characteristics of active pharmaceutical ingredients and application of supersaturatable dosage forms for improving bioavailability of poorly absorbed drugs." *Adv Drug Deliv Rev* 64(6):480–495.

New chemical entities are required to possess physicochemical characteristics that result in acceptable oral absorption. However, many promising candidates need physicochemical modification or application of special formulation technology. This review discusses strategies for overcoming physicochemical problems during the development at the preformulation and formulation stages with emphasis on overcoming the most typical problem, low solubility. Solubility of active pharmaceutical ingredients can be improved by employing metastable states, salt forms, or cocrystals. Since the usefulness of salt forms is well recognized, it is the normal strategy to select the most suitable salt form through extensive screening in the current developmental study. Promising formulation technologies used to overcome the low solubility problem include liquid-filled capsules, self-emulsifying formulations, solid dispersions, and nanosuspensions. Current knowledge for each formulation is discussed from both theoretical and practical viewpoints, and their advantages and disadvantages are presented.

Kerns, E. H. et al. (2008). "In vitro solubility assays in drug discovery." *Curr Drug Metab* 9(9):879–885.

The solubility of a compound depends on its structure and solution conditions. Structure determines the lipophilicity, hydrogen bonding, molecular volume, crystal energy and ionizability, which determine solubility. Solution conditions are affected by pH, co-solvents, additives, ionic strength, time and temperature. Many drug discovery experiments are conducted under "kinetic" solubility conditions. In drug discovery, solubility has a major impact on bioassays, formulation for in vivo dosing, and intestinal absorption. A good goal for the solubility of drug discovery compounds is >60 ug/mL. Equilibrium solubility assays can be conducted in moderate throughput, by incubating excess solid with buffer and agitating for several days, prior to filtration