

Solubility Assay by Laser Nephelometry

Background: This is a high-throughput and affordable option for rapid evaluation of kinetic solubility for a large number of compounds in any aqueous buffer. Linear serial dilutions of each compound to be analyzed are prepared from DMSO stock solutions in an aqueous buffer of the specified composition and pH, and the approximate precipitation points for each compound are determined from the light scatter graphs (working solubility range is from 50-100 μM up to 1-2 mM). This assay is typically performed in duplicates. For a rough estimate of aqueous solubility (“solubility not lower than...”), this method can be simplified: instead of linear serial dilutions, light scattering can be measured at one or two concentrations of compounds (high-throughput solubility threshold method). Those compounds yielding light scattering signal values significantly higher than that of the highly soluble compound (2'-deoxy-5-fluorouridine) are considered insoluble at tested concentrations. As a control, a reference compound poorly soluble at the same concentrations is used.

Service Details: For the light scattering measurements we use BMG Labtech Nephelostar laser microplate nephelometer, which operates with 96- or 384-well plates. We typically perform high-throughput solubility threshold assay in singletons at up to 2 mM compound concentrations with Ondansetron as a poorly soluble reference and deoxyfluorouridine as a well soluble one. This method can be modified upon request.

Deliverable: Compounds solubility normalized to deoxyfluorouridine (100% soluble) and Ondansetron (0% solubility) is calculated. Selected ranges of Relative Solubility (>0.8 , $0.6-0.8$ and <0.6) allow dividing compounds in clearly distinguishable groups (good solubility, intermediate solubility and poor solubility) at the chosen solubility threshold. Full study report is provided.

Sample Submission: Typically, a minimal accurately weighable quantity of dry compound (~ 1 mg or 2 μmol) or 50 μL of 20 mM stock DMSO solution) is required for this assay. However, the exact required amount would depend on the solubility range of interest.