Drug Physicochemical Properties

Determination of water and thermodynamic solubility

Determination of physicochemical properties is one of the first stages in non-clinical drug discovery and development. Among the main physicochemical properties, solubility stands out, and has a major impact on bioassays, formulation for *in vivo* dosing, and intestinal absorption [1]. In this sense, solubility is a critical property for drug discovery, which may affect the chances of a candidate molecule to reach clinical trials of drug development and to be launched in the market.

Test System: Water or solutions with pH 2.2 and 6.8

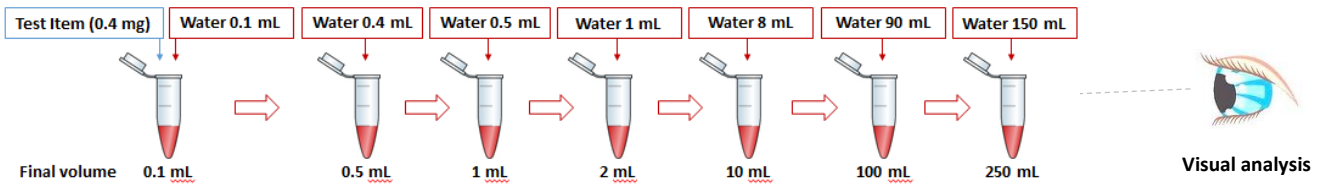
Reference Item: Upon request

Experimental number: Duplicate

Main read-outs: Visual analysis;
Test item quantification by UHPLC-MS

PS: Prior to the evaluation of chemical stability, the development and validation of the analytical method for the test item are indispensable prerequisites.

Water Solubility

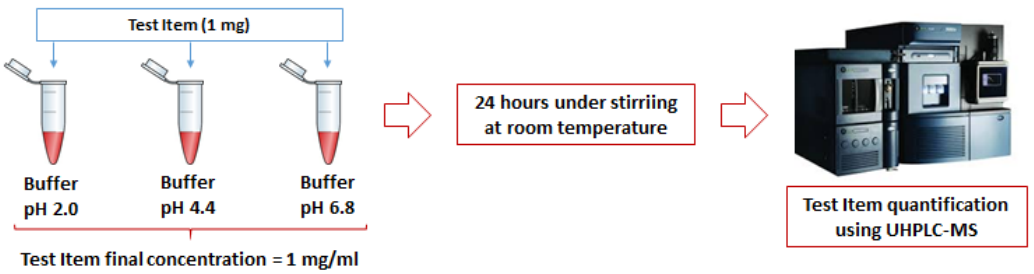


Item Test (0.4 mg)

Water (mL)	Final volume (mL)	Final concentration (mg/mL)	Solubilized
0.1	0.1	4.0	Not
0.4	0.5	0.8	Not
0.5	1	0.4	Not
1	2	0.2	Not
8	10	0.04	Not
90	100	0.004	Not
150	250	0.0016	Not

Figure 1. Experimental design for aqueous solubility determination according to OECD 105 [2]. Results demonstrated that item test was not soluble in water in any of final concentration tested. According to OECD 105 , when more than 100 mL of water is required to solubilize 0.1 grams of teste item, its aqueous solubility is said to be less than 1 g/L..

Thermodynamic Solubility



Test Item (0.4 mg/mL)	Test Item Concentration (mg/mL)	Nominal Concentration (mg/mL)	% bias
pH 2.2	0,01061	0,4	2,65
pH 4.4	0,00540	0,4	0,54
pH 6.8	Not Detected		

Figure 2. Experimental design for thermodynamic solubility determination according to OECD 105. Results demonstrated that test item concentration in pH 2.0 and 4.4 were, respectively, 2,65% and 0.54% of the nominal concentration. In ph. 6.8 the test item was not detected. These results corroborate the results obtained in the water solubility test and indicates that the test item presents low aqueous solubility.

References:
[1] Kerns, E. H., Di, L. Drug Like Proprieties: Concept, Structure Design and Methods from Toxicity Optimization Press: Elsevier, London, UK, 2016.
[2] OECD 105. OECD GUIDELINE FOR THE TESTING OF CHEMICALS Water Solubility.

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