Drug Physicochemical Properties

Determination of Drug Lipophilicity

Lipophilicity comprehends a physicochemical property of principal importance in drug discovery and development. Lipophilicity determines solubility, reactivity and degradation of drugs, as well as formulation of pharmaceuticals. Moreover, lipophilicity is important for drug biological activity, especially for its pharmacokinetic and pharmacodynamic [1]. Experimentally, drug lipophilicity is determinated as Partition Coefficient in two immiscible solvents, ususally, n-octanol/water [2].

Test System: Octanol/Water solution

Reference Item: Upon request

Experimental number: Triplicate

Main read-outs: Test item quantification by UHPLC-MS

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

Validation Data

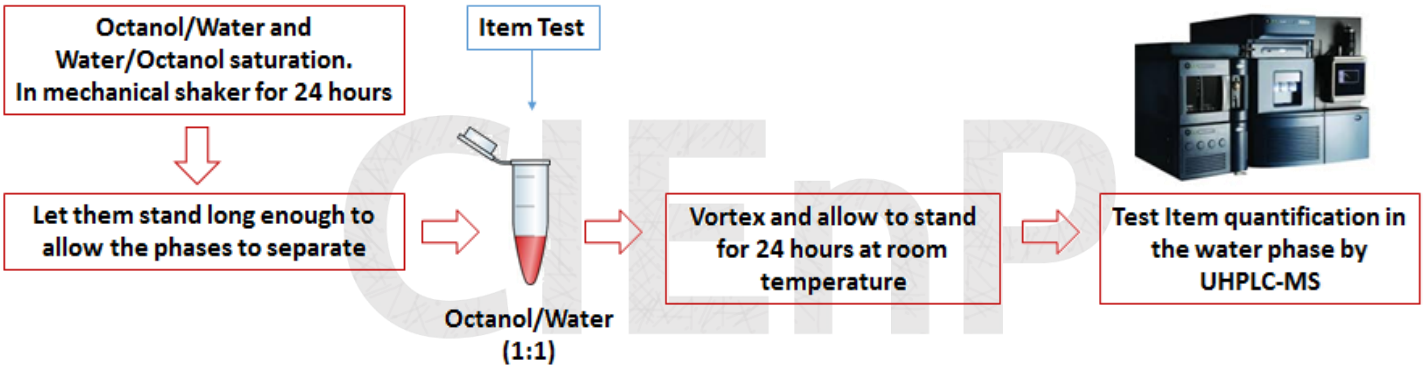

Figure 1. Experimental protocol for drug partition coefficient (n-octanol/Water) determination. Firstly, the two solvents are mutually saturated at the temperature of the experiment for 24 hours on a mechanical shaker, and then to let them stand long enough to allow the phases to separate. After, test item is prepared using one part of n-octanol (saturated in water) and one part of water (saturated in n-octanol). Samples are vortex and allow to stand for 24 hours at room temperature. Then, water phase is collected for item test quantification by UHPLC-MS. Analysis is performed in triplicate.

Test item starting concentration	Test item concentration in water phase (µg/mL)	Test item concentration in n-octanol phase(µg/mL)	[Octanol]/[water] (Partition coefficient)	Log P
400 µg/mL	0.05	399.95	7999	3.90

Figure 2. Test Item quantification in water phase by UHPLC-MS, using an analytical method properly developed and validated. Test item concentration in n-octanol phase is calculated subtracting the concentration obtained in water phase from the starting concentration. Log P represents the drug partition coefficient in n-octanol/water and indicates test item lipophilicity.

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 107. OECD GUIDELINE FOR THE TESTING OF CHEMICALS. Partition Coefficient (n-octanol/water): Shake Flask Method.

Contact us: +55 (48) 3261-2856 / contato@cienp.org.br