

pK_a and log P

Background Information



' pK_a affects solubility, permeability, log D and oral absorption by modulating the distribution of neutral and charged species.'

¹Di L and Kerns EH. (2003) *Current Opinion in Chemical Biology* 7; 402-408.

- The pK_a is the pH at which the molecule is 50% protonated.
- Log P (or partition co-efficient) is a measure of the lipophilicity of a compound.
- Cyprotex's pK_a and log P determination uses UV-metric and pH-metric technology developed by Sirius, which is considered to be a 'gold standard' method for determining these properties.
- In UV-metric methods, the pK_a is measured by analysing changes in multi-wavelength UV spectra during acid-based titration of the sample. UV-metric pK_a methods work for compounds with pH-sensitive chromophores.
- In pH-metric methods, pK_a is measured by titrating a solution of the sample in water or solvent with acid and base, and calculating the pK_a from the shape of the titration. pH-metric methods work for any ionisable compound, but require more sample than UV-metric methods.
- The pH-metric method is also used to measure log P in a two-phase acid-base titration in the presence of octanol.

Protocol

Method

Fast UV titration for pK_a
UV-metric titration for pK_a
Potentiometric (pH-metric) titration for pK_a and log P

Instrument

SiriusT3

Test Article Requirements

3-5 μ L of 10 mM stock solution (UV-metric)
1 mg solid compound (pH-metric)

Partition Solvent used for

Log P Determination

n-Octanol (others available on request)

Data Delivery

pK_a
log P (optional)
Standard error
RMSD
Calculated log D at $pH_{7.4}$
(based on pK_a and log P)

