

Physicochemical Parameters for QSAR

Experiment 4 - Practical Notes

Name: _____ Roll no.: _____ Date: _____

Aim

To calculate partition, ionisation and molar-refractivity parameters from assigned data.

Principle

QSAR uses defined descriptors to relate chemical structure and measured activity in an explicit dataset. A descriptor or correlation alone does not prove a biological mechanism.

Requirements

- Supplied equilibrium concentration, pKa, density, refractive-index and activity datasets; calculator or spreadsheet.

Procedure

1. Partition coefficient

Use neutral-species equilibrium concentrations in the stated immiscible phases and calculate P and logP. Distinguish pH-dependent distribution D from neutral-species partition P.

2. Ionisation

Use the assigned pKa and pH model for the acid or base; record which chemical species the fraction refers to.

3. Molar refractivity

Apply the Lorentz-Lorenz equation using refractive index, formula mass and density on consistent units.

4. Compare descriptors

Prepare a compound-by-descriptor table and examine the assigned relationship with activity, noting dataset size and confounding.

5. Report

State descriptor definitions, units, conditions and the limits of an observed correlation.

Observations and Record

Descriptor	Input	Calculated result
P / logP	_____	_____
pKa / ionisation fraction	_____	_____
Molar refractivity	_____	_____
Activity relationship	_____	_____

Worked Example

The numbers below are illustrative; enter your own observations in the record.

- $P = \text{Corganic(neutral)} / \text{Caqueous(neutral)}$; $\log P = \log_{10}(P)$. Example: $20/2 = 10$, so $\log P = 1$.
- For a monoprotic weak acid, ionised fraction = $1/[1 + 10^{(pK_a - pH)}]$. At $pH = pK_a$, it is 0.5. For a base, the protonated fraction = $1/[1 + 10^{(pH - pK_a)}]$.
- Molar refractivity = $[(n^2 - 1)/(n^2 + 2)] \times M/\rho$. Example: $n = 1.5$, $M = 100 \text{ g/mol}$ and $\rho = 1 \text{ g/cm}^3$ give $29.41 \text{ cm}^3/\text{mol}$.

Result

Record the completed observations, calculations and conclusion with units. State any limitation of the observation.

Precautions

- State phase composition, pH and temperature; do not compare undefined partition measurements.
- Use an appropriate ionisation model rather than applying a monoprotic relation to every compound.

Viva Questions and Answers

1. How do logP and logD differ?

LogP describes neutral-species partitioning; logD includes the distribution of species at a stated pH.

2. Does a QSAR association prove mechanism?

No. It must be validated and interpreted within the model and dataset.

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