Kinetics and Drug Stability

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Pseudo-order reactions:

Simplify the kinetics of complex reactions
Rate laws become easier to work with.

\[
\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5 + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CO}_2\text{H} + \text{C}_2\text{H}_5\text{OH}
\]

• If the concentration of water does not change appreciably during the reaction.
  – Rate law appears to be first order.

• Typically hold one or more reactants constant by using high concentrations and low concentrations of the reactants under study.
The decomposition of a compound in solution follows 1st order according to the following equation:

\[- \frac{d (C)}{dt} = K_1(C)\]

If the concentration of the drug in a product exceeded its maximum solubility (e.g. in suspension products).

The concentration of reactant in solution remain constant as long as there is excess solid present.

This concentration of course equals the saturation solubility of the drug in the specified solvent.
**Apparent Zero-Order Kinetics (Suspensions)**

\[- \frac{d\ (C)}{dt} = K_1 S\]

\[- \frac{d\ (C)}{dt} = K_0\]

Where

\[k_o = k_1 \ C\]

or

\[k_o = k_1 \ S\]

Where S is the Saturation Solubility of the drug in that solvent and \(k_1\) is its 1\(^{st}\) order rate constant.
Example

A prescription for a liquid aspirin preparation is called for 325 mg/ 5ml. The solubility of aspirin at 25 °C is 0.33g /100ml; the 1st order rate constant for aspirin degradation in the solution is 4.5 x 10^-6 sec^-1. Determine the shelf life (t_{90%}) for the liquid prescription at 25 °C.
Apparent Zero-Order Kinetics (Suspensions)

Example

A prescription for a liquid aspirin preparation is called for 325 mg/5ml. The solubility of aspirin at 25 °C is 0.33g/100ml; the 1st order rate constant for aspirin degradation in the solution is $4.5 \times 10^{-6}$ sec$^{-1}$. Determine the shelf life ($t_{90\%}$) for the liquid prescription at 25 °C.
Concentration of aspirin in 100 ml of the preparation =

\[
\frac{325}{1000} \times \frac{100}{5} = 6.5 \text{ g /100 ml}
\]

Which is much higher than the solubility of aspirin at 25 °C (0.33 g/100ml),

\[\therefore\] The preparation is definitely a suspension and follows an apparent
zero order kinetics, where the shelf life equals: \((0.1 \ C_o)/ \ k_o\).

\[
k_o = k_1 \cdot S = (4.5 \times 10^{-6} \text{ sec}^{-1}) \times (0.33 \text{ g /100ml})
\]

\[= 1.5 \times 10^{-6} \text{ g /100ml} \cdot \text{sec}^{-1}\]
Pseudo-first order reactions

\[ A + B \quad \rightarrow \quad C + D \]

If B was the solvent and so its concentration remains almost constant since it is present in such great excess.

\[ R_f = - \frac{dA}{dt} = - \frac{dB}{dt} = k (A)(B) \quad - \quad \frac{d(A)}{dt} = K' (A) \]

\[ K' = K (B) \]
Knowing that certain drug undergoes first order degradation, explain **WHY**

It is better to prepare its suspension in the form of drop products rather than oral suspension.

5mg/0.5ml

5mg/5ml