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Short Communication

Derivation of the pH-Dependent Higuchi Equation

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Abstracts

We have converted the diffusion-controlled Higuchi equation to pH-dependent form in this paper. We have modified the original Higuchi equation to produce the pH-dependent variant by incorporating the Nernst-Planck equation into Flick's first law. A time-dependent medication particle delivery from a silica matrix might be predicted using the modified equation.

Keywords: Higuchi equation; Flick's first law; Nernst-Plank equation; Drug delivery; pH-dependent

Introduction

Since Higuchi [1] deduced the drug delivery rate for the first time in 1961, the application of mathematical modelling to create regulated and sophisticated drug delivery systems has opened up new avenues in the field of pharmaceutical science [2-4]. In recent years, this paradigm has been the subject of extensive research [1, 5-13]. The model accounts for the excess loading of a drug particle into a carrier matrix above its solubility limit. Flick's first law states that due to the gradient in concentration, when the assembly is dissolved into the fluid, which is regarded as a sink, the drug particles are drastically released into the surrounding fluid [14]. According to Higuchi's theory, which is illustrated in Figure 1 and known as the 'moving boundary approach', [15] the boundary of the concentration gradient moves in the opposite direction of the stream of drug particles. The speed at which the gradient's concentration boundary moves determines how quickly drug particles migrate. Higuchi arrived at the following two equations based on this theory [1]:

$$M = \sqrt{Dc_s\left(2A - c_s\right)t} \quad (1)$$

$$\frac{\partial M}{\partial t} = \sqrt{\frac{Dc_s\left(A - \frac{1}{2}c_s\right)}{2t}} \quad (2)$$

In Eqs (1) and (2), A represents the surface area of the matrix, c_0 and c_s represent the initial and saturated concentrations of solute drug particles in the matrix, and D represents the diffusion of particles in the matrix. M represents the cumulative mass of solute accumulated in the surrounding fluid in time from A 's surface area. Here, we attempted to derive the pH-dependent variant of the Higuchi equation. The resulting equation will be helpful to examine experimental findings of pH-dependent drug loading and release by carrier matrix (Figure 1).

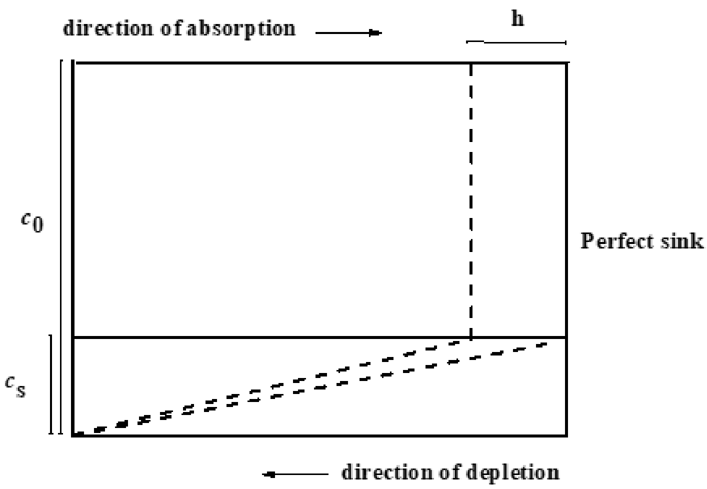

Figure 1: The Higuchi model's schematic illustration illustrating the drug flow and depletion directions.

Derivation

The following eq (3) is applicable if A is the area, M is the total mass of drug particles accumulated over time t, c_o, is the starting drug concentration in the matrix, and c_s is the maximum quantity of drug that can be dissolved in the matrix.

$$M = Ah\left(c_0 - \frac{c_s}{2}\right) \quad (3)$$

The drug flux, J would switch from $J = \frac{\partial M}{A\partial t}$ to

$$J = \left(c_0 - \frac{c_s}{2}\right)\frac{\partial h}{\partial t} \quad (4)$$

The Nernst-Planck equation [16] extends Flick's law of diffusion [17] of particle flux, J resulting from concentration gradient, $\frac{c_s}{h}$, to charged particles arising from electric potential gradient, $\frac{zDe\psi m}{h}$, where z_D is the valency of the charged particle, e is the elementary electron charge, and ψ_m is the electric potential. The formula for the particle's total flow is

$$J = D\frac{c_s}{h} + \frac{zeDc_s}{k_B T}\frac{\psi}{h} \quad (5)$$

Adding up eqs (4) and (5)

$$\left(c_0 - \frac{c_s}{2}\right)\frac{\partial h}{\partial t} = D\frac{c_s}{h} + \frac{Dc_s}{k_B T}\frac{E^{ES}}{h} \quad (6)$$

$$\left(c_0 - \frac{c_s}{2}\right)h\partial h = Dc_s\left(1 + \frac{E^{ES}}{k_B T}\right)\partial t \quad (7)$$

When eq (7) is integrated, the result is

$$\left(c_0 - \frac{c_s}{2}\right)\frac{h^2}{2} = Dc_s\left(1 + \frac{E^{ES}}{k_B T}\right)t + K \quad (8)$$

where K is the integration constant. Applying the boundary condition results in i.e., when $t = 0,\ h = 0$.

$$h = \sqrt{\frac{2Dc_s\left(1 + \frac{E^{ES}}{k_B T}\right)t}{\left(c_0 - \frac{c_s}{2}\right)}} \quad (9)$$

and $K = 0$. The result of substituting the h value from eq (9) into eq (8) is

$$M = A\sqrt{2Dc_s\left(1+\frac{E^{ES}}{k_BT}\right)\left(c_0-\frac{c_s}{2}\right)t} \quad (10)$$

Equation (10) reduces to

$$M = A\sqrt{2Dc_0c_s\left(1+\frac{E^{ES}}{k_BT}\right)t} \quad (11)$$

for $c_0 \gg c_s$. Eq. (11) is reduced to

$$M = A\sqrt{2Dc_0c_st} \quad (12)$$

which is the original diffusion-controlled Higuchi equation, when the migration of particles with no charge occurs [1]. Diffusion controls the first term, $2Dc_0c_s$ in eq (11), while pH controls the second term,

$2Dc_0c_s\frac{E^{ES}}{k_BT}$. While a negative value of $1+\frac{E^{ES}}{k_BT}T$ T

indicates adsorption or loading of drugs in the matrix, a positive value of $1+\frac{E^{ES}}{k_BT}$ indicates desorption or release of drugs from the matrix that accumulate into the sink. Thus, the expression $1+\frac{E^{ES}}{k_BT}$ aids in the prediction of drug loading and release that is pH dependent.

Conclusion

The diffusion-regulated Higuchi equation has been derived to result in pH-dependent medication release from drug carrier. This is achieved by include the potential gradient migration of the Nernst-Planck equation in the Higuchi model. This equation will be helpful for a qualitative preliminary evaluation of pH-dependent medication release from a carrier. We are currently working to confirm the proposed equation with experimental data.

Conflict of Interest

No conflicts of interest are disclosed by the authors.

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