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Importance and application of first order development of new compound in pharmacy

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Abstract
Drug photodegradation data are usually treated by zero-, first- or second-order kinetic equations. Such treatments would lack reliability since the aforementioned equations have been originally developed for pure thermal reactions. In this respect, it has recently been shown that unimolecular photodegradations obey Φ-order kinetics (Maafi and Maafi, 2013). However, no similar information is, thus far, available for other reactions including photoreversible AB(2Φ) systems. This paper aims at filling this gap for AB(2Φ) kinetics.
As the human body ingests substances and medications, it utilizes a variety of metabolism and elimination processes. The second focus of this topic is zero and first-order kinetic elimination, which is clinically useful in achieving a therapeutic level of medication and prognostically assessing toxicity levels and implementing treatment. For simplicity, the following discussion is specific to a one-compartment model, which views the human body as a homogeneous unit. Lastly, while most drugs undergo elimination via first-order kinetics, a firm understanding of both zero and first-order kinetics is crucial in a clinical setting, as there can be fluidity between the 2 types of elimination with the same specific substance (see **Graph.** Zero- and First-Order Elimination and Equations).[1]

I. Importance

Determination and understanding of how a particular substance is eliminated are important when administering medications to achieve a therapeutic level and when assessing a patient who ingested a toxic substance. Specifically, regarding toxicology, if the ingested substance is unknown to the patient and practitioner, routine blood/plasma testing of the substance and analysis of the decline in concentration aids in identifying the ingested substance. For example, suppose the substance follows a zero-order elimination. In that case, the amount eliminated depends on time and not the amount ingested, in contrast to first-order kinetics, in which the amount eliminated depends on the maximum blood/plasma concentration and not on time. Furthermore, once the substance and its properties are understood, proper treatment may be given to a patient who ingested a toxic substance.

To achieve the desired therapeutic level of a medication, a clinician must understand the elimination order and utilize the information in subsequent dosing to maintain the therapeutic concentration over a set period. Misunderstanding of kinetic elimination may lead to patients experiencing toxic symptoms and could lead to other iatrogenic adverse effects up to and including death.

The fundamental difference between zero and first-order kinetics is their elimination rate compared to total plasma concentration. Zero-order kinetics undergo constant elimination regardless of the plasma concentration, following a linear elimination phase as the system becomes saturated. A simple analogy would be an athlete signing an autograph on a picture. Regardless of the number of photographs that must be signed, the athlete can only sign 1 autograph every 15 seconds. The rate-limiting factor of this analogy and zero-order kinetics is time.

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First-order kinetics proportionally increases elimination as the plasma concentration increases, following an exponential elimination phase as the system never achieves saturation. Furthermore, when attempting to obtain a therapeutic level of plasma concentration or regarding drug toxicity, one must utilize their knowledge of a particular drug elimination kinetic. The entire team can sign the photographs to utilize the same analogy. The more photographs there are to sign, the more athletes can sign. The initial concentration is the rate-limiting factor of this analogy and in first-order kinetics.

In the case of autographs, if the number of needed autographed photos exceeds the number of available athletes, the first-order elimination becomes zero-order. As described above, the system of first-order kinetic elimination can become saturated, forcing a zero-order kinetic model to take place. Once the concentration falls below a certain level, a first-order kinetic elimination is again seen as the system is no longer saturated.[2][3][4]

II. Application

Both zero and first-order kinetics derive from the same equation. As seen in "Equation No. 1 "Kinetic order elimination equation," where delta [drug] represents the change in plasma concentration of the drug divided by time, "n" represents either first or zero-order elimination with 1 or 0, respectively, and "-Kc" represents a constant. For example, when n = 1, the change in drug plasma concentration divided by time is proportional to the amount of drug initially given, showing the rate-limiting factor being the initial concentration. In contrast, when n = 0, $[Drug]^0 = 1$, the change of drug plasma concentration is equal to the constant, -Kc. Thus demonstrating how the rate-limiting factor is time.

The same principles with zero and first-order kinetics are demonstrable on a graph. As seen in "Graph 1: Zero-order kinetics", regardless of the plasma concentration of a substance, the same amount is limited over 2 hours. Thus, the graph demonstrates a linear slope. Compared to "Graph 2: First-order kinetics," the exponential curve of the graph illustrates how a larger plasma concentration implies a larger amount eliminated in 2 hours.[5][6]

When administering medications, one must fully understand the mechanism of action and elimination to reduce unwanted adverse effects. Furthermore, when assessing a patient who may have either intentionally or accidentally ingested a toxic quantity of a substance, knowing that the substance's elimination properties aid treatment and the disease course

First order elimination kinetics
A definition of this concept can be borrowed from the college answer to Question 5(p.2):
"First-order kinetics... is where a constant fraction of drug in the body is eliminated per unit of time"
This is a logarithmic function. All enzymes and clearance mechanisms are working at well below their maximum capacity, and the rate of drug elimination is directly proportional to drug concentration.

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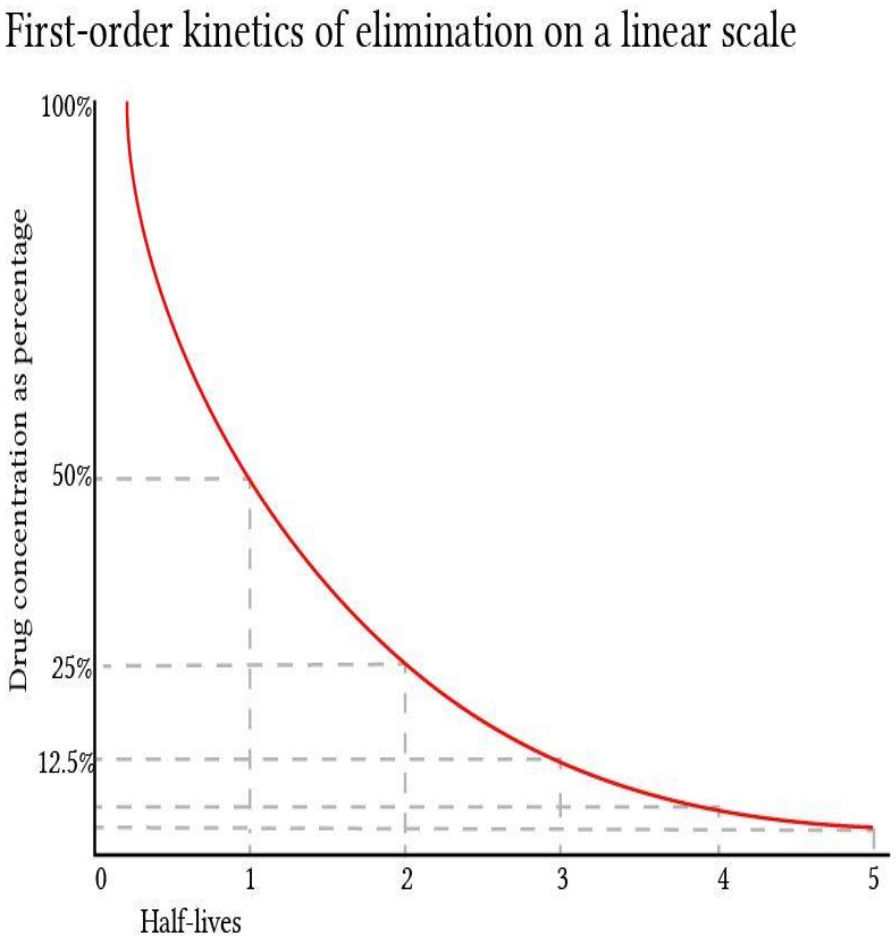
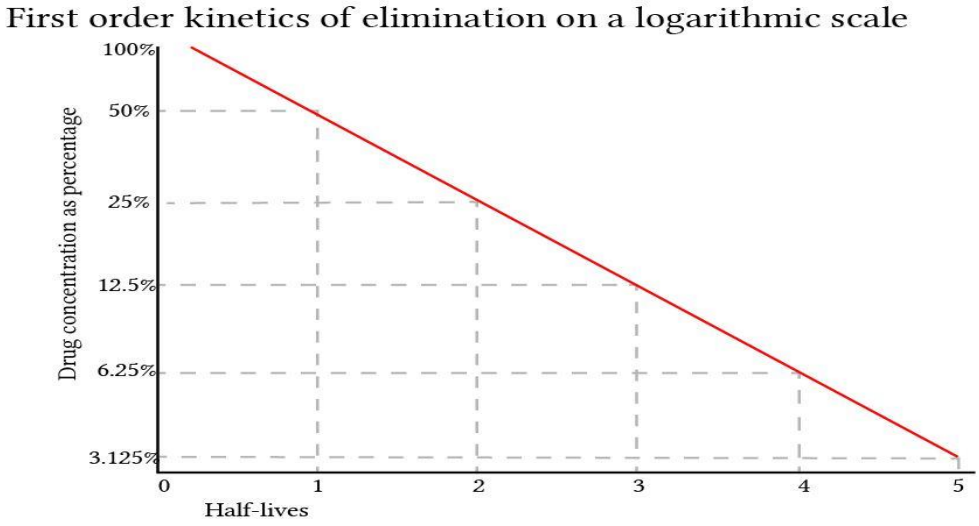


The drug concentration halves predictably according to fixed time intervals. When you plot this on a semi-logarithmic scale, the relationship of concentration and time is linear.



If you plot the relationship of concentration vs. elimination rate, the same sort of linear relationship is seen:

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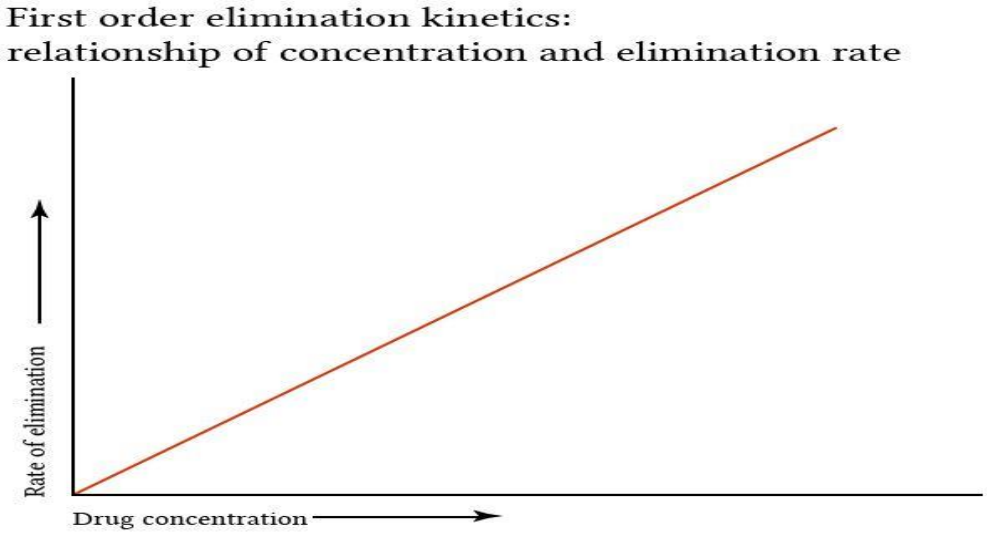

The term "first order" actually comes from chemistry, where is has classically been used to describe reaction kinetics. When doubling the concentration of reagents also doubles the reaction rate, the increase in rate is by a factor of 2 (2 to the first power, or 2^1). That "first power" gives rise to the term "first order". In that fashion, one can have a "second order" reaction where doubling the concentration of reagents *quadruples* the reaction rate (i.e 2 to the second power, 2^2). Following this trend in nomenclature to its most absurd extent, third-order fourth-order and fiftieth-order reactions can be conceived of.

III. Conclusion

Zero-order drug delivery devices offer the potential to precisely tune release kinetics to prolong drug concentrations within the therapeutic window. As a result, these systems can improve drug efficacy, reduce side effects, and reduce the frequency of administration, which can all contribute to improved patient compliance and disease management. However, the most appropriate drug delivery system for a particular indication depends on a number of factors including: (1) the drug half- life, therapeutic window, and dose size; (2) the severity of both the disease itself and the side effects of exceeding the MTC; (3) the duration of the therapy (i.e., chronic vs acute); and (4) the frequency and inconvenience of existing therapies. The ideal drug delivery system for most chronic diseases would be easy-to-administer, inexpensive, and achieve consistent drug concentrations within the therapeutic window for a prolonged period of time at the site of therapeutic benefit. Oral or topical delivery methods are often preferred by patients but have inherent challenges that need to be overcome to achieve long-term release. For oral systems, improved residence time and consistency are key challenges, in addition to the poor oral bioavailability of some drugs, particularly macromolecules. True zero-order drug delivery systems have been limited to large and expensive devices that are not attractive for most use cases because of their high cost, limited duration, and inconvenient use, which can require surgery. Implantable pump systems certainly have the ability to achieve consistent drug release for long periods of time but are only useful for a small subset of patients and diseases due to their high cost and need for surgical implantation. On the opposite end of the spectrum are microneedles and hydrogels, which are easily administered but have not achieved zero-order release; additional work is required to improve these systems' release kinetics before they can be used to control the release of drugs with small therapeutic windows. One promising system achieved transdermal delivery of rivastigmine, a drug used to treat Alzheimer's and Parkinson's disease, from electro-responsive poly(acrylamide)-grafted- dextran and poly(acrylamide)-grafted-pullulan hydrogels [280,281]. Application of electrical stimulation enhanced drug permeatio

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