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# CLINICAL SIGNIFICANCE OF HALF LIFE OF DRUGS

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**ABSTRACT**

Half life of drug is a pharmacokinetic property of the drug. For any given drug and dose, the plasma concentration of the drug will rise and fall according to the rates of three processes: absorption, distribution, and elimination**.** The half-life of a drug is the time it takes for its concentration in blood or plasma to decrease by half. The time required for any plasma concentration of drug to fall by 50% is known as half- life of that drug ($T_{1/2}$). In this review we summarized about the half-life of the drug.

**Key words:** Pharmacokinetics, Half-life, Drug.

## INTRODUCTION

Pharmacokinetics is the study of drug disposition in the body and focuses on the changes in drug plasma concentration. For any given drug and dose, the plasma concentration of the drug will rise and fall according to the rates of three processes: absorption, distribution, and elimination**.** Absorption of a drug refers to the movement of drug into the bloodstream, with the rate dependent on the physical characteristics of the drug and its formulation. Distribution of a drug refers to the process of a drug leaving the bloodstream and going into the organs and tissues. Elimination of a drug from the blood relies on two processes: biotransformation (metabolism)of a drug to one or more metabolites, primarily in the liver; and the excretion of the parent drug or its metabolites, primarily by the kidneys. It can be calculated from the elimination rate constant, but it is usually determined from the plasma drug concentration curve. The half-life of a drug is the time it takes for its concentration in blood or plasma to decrease by half. The time required for any plasma concentration of drug to fall by 50% is known as half- life of that drug ($T_{1/2}$) [1-3]. We usually consider the half life of a drug in relation to the amount of the drug in plasma. A drug's plasma half-life depends on how quickly the drug is eliminated from the plasma. A drug molecule that leaves plasma may have any of several fates. It can be eliminated from the body, or it can be translocated to another body fluid compartment such as the intracellular fluid or it can be destroyed in the blood. For drugs that display multiple half-lives, an important consideration is determining which half-life is more important from a pharmacological, toxicological, or pharmacokinetic standpoint. This can be assessed by comparing the AUC of each phase relative to the total AUC; i.e., determining under which half-life the majority of exposure occurs. Additionally, if efficacious (or toxic) doses and resulting concentrations of a drug are known, one may ascertain which phase exhibits the more clinically important half-life. Half-life can be used to determine the appropriate dosage interval to achieve a target concentration time profile.

## CLINICAL FACTORS AFFECTING HALF LIFE

The half-life can also be expressed in terms of the drug's clearance and volume of distribution, indicating that the drug's half-life will change when either of these factors is altered. Disease, age, and other physiologic variables can alter drug clearance or volume of distribution and thereby change the elimination half-life. Many factors are affecting the half life of drug.

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If there is any abnormality in patient, it alters half life. In this case dose management of drug is required. The removal of a drug from the plasma is known as clearance.The distribution of the drug in the various body tissues is known as the volume of distribution**.** Both of these pharmacokinetic parameters are important in determining the half life of a drug [4].

**INCREASING FACTORS**

The factors which are able to increase the half life of the drug. They may be several in number as Diminished renal plasma flow or hepatic blood flow (in cardiogenic shock, heart failure, or hemorrhage); Decreased extraction ratio (as seen in renal disease); Decreased metabolism (when another drug inhibits its biotransformation or in hepatic insufficiency, as with cirrhosis) [5].

Agents which have half-life's longer than the usual dosing interval would be expected to accumulate and reach a plateau. Some agents have a half-life such that they would accumulate even if given once a week. They are clearly once-a-day medications. It has always been a puzzle that patients will appear taking medications such as diazepam (t½ = 24-48 hours) t.i.d. or even q.i.d. or amitriptyline (t½ = 2-5 days) t.i.d. Both of these agents would be expected to have the same effects given once-a-day. Using this same information, it is not surprising (the phenomena of tolerance) that flurazepam (t½ = 48-90 hours) loses it's effectiveness as a sleeping pill with time [6].

**DECREASING FACTORS**

The factors which are able to decrease the half-life of the drugs are increased hepatic blood flow; decreased protein binding; Increased metabolism [7].

**CLINICAL IMPORTANCE**

In clinical research, the half-life is needed and used to determine how long after the dosing of the test agent that one is required to take blood samples so that the area under the time course curve (AUC) represents the true time course of the drug. In general, agents with very short t½'s will require an intravenous infusion to maintain the continued presence of the drug. Examples include lidocaine and dopamine. Other agents with a short half-life are knowingly given at intervals longer than 5 times their plasma t½ either because the continued presence of the drug is not required for receptor activity or because the effect of the drug outlasts the plasma concentration. The organic acid antibiotics fall into the former group [8]. The later group is large and brings up the concept of an effect (efficaciousness) half-life. What usually happens is that it is noticed that a drug with a relatively short half-life is still able to produce an effect long after it is supposedly eliminated (which would be 5 times the plasma half-life). It is presumed that the drug is acting intracellularly and either remains partly bound to the receptor long after most of the extracellular drug has been eliminated orthe drug is a "hit-and -run" type which alters a receptor such that the effect remains long after the drug is gone. The reason it is important to always be on the lookout for this phenomenon is that it is far easier for patients to take a drug once or twice a day than three of four times a day [9-13].

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