CHAPTER 1

Introduction to Pharmacology

CHAPTER FOCUS

This chapter provides an introduction to basic pharmacology. It also describes the properties of drugs, their sources, how drugs produce effects, and drug nomenclature.

CHAPTER OBJECTIVES

After studying this chapter, you should be able to

- define pharmacology and its major subdivisions.
- describe what a drug is and explain the differences between a therapeutic effect, side effect, and toxic effect.
- identify a drug receptor and trace how agonists and antagonists interact with receptors.
- explain the relationship between drug dosage and drug response, and the relationship between drug response and time.
- explain drug safety and therapeutic index.
- describe three names by which drugs are known.
- list two common drug reference books.

CHAPTER TERMINOLOGY

adverse effect: undesirable side effect.

agonist: drug that binds to its receptor and produces a drug action.

antagonist: drug that binds to its receptor and prevents other drugs or substances from producing an effect.

chemical name: name that defines the chemical composition of a drug.

controlled substance: drug that has the potential for abuse and thus is regulated by law.

dose: exact amount of a drug that is administered in order to produce a specific effect.

drug: chemical substance that produces a change in body function.

ED50: effective dose 50, or dose that will produce an effect that is half of the maximal response.

generic name: nonproprietary, or common, name of a drug.

LD50: lethal dose 50, or dose that will kill 50% of the animals tested.

mechanism of action: explanation of how a drug produces its effects.

nonprescription, over-the-counter (OTC) drug: drug that can be purchased without the services of a physician.

pharmacology: study of drugs.

potency: measure of the strength, or concentration, of a drug required to produce a specific effect.

prescription drug: drug for which dispensing requires a written or phone order that can only be issued by a licensed physician.

product name: proprietary name of drug given when marketed by a pharmaceutical company.

receptor: specific location on a cell membrane or within the cell where a drug attaches to produce its effect.

Schedule I drug: drug with high abuse potential and no accepted medical use.

Schedule II drug: drug with high abuse potential and accepted medical use.

Schedule III drug: drug with moderate abuse potential and accepted medical use.

Schedule IV drug: drug with low abuse potential and accepted medical use.

Schedule V drug: drug with low abuse potential and accepted medical use; can be administered by a licensed pharmacist.

side effect: drug effect other than the therapeutic effect that is usually undesirable but not harmful.

site of action: location within the body where a drug exerts its therapeutic effect, often a type of specific receptor.

therapeutic effect: desired drug effect to alleviate some condition or symptom of disease.

therapeutic index (TI): ratio of the LD50 to the ED50.

toxic effect: undesirable drug effect that can be harmful or life-threatening.

Pharmacology is the study of drugs. A drug can be any substance that, when administered to living organisms, produces a change in function. Thus, substances such as water, metals (iron), or insecticides can be classified as drugs. However, the term *drug* commonly means any medication that is used for treating disease.

Pharmacology refers to a very broad area of study. It can be broken down into several topics, each one a major subject area of study. Table 1.1 lists each of these areas. Throughout this book, tables organize information so that the pharmacology of each drug class can be easily understood.

A logical question to ask about pharmacology is "Where do drugs come from?" There are several sources of drugs. In the early days of medicine, most drugs were obtained from plant or animal sources. Plants and organisms may contain active substances that can act as drugs. Some drugs—such as morphine, digitalis, and insulin—are still derived from these sources. However, most drugs today are synthesized in pharmaceutical manufacturing plants.

Another basic question that should be answered is "What actually is a **drug?**" Every pure drug is a chemical compound with a specific chemical structure. Because of its structure, a drug has certain properties that are usually divided into chemical properties and biological properties. The properties of any drug determine what effects will be produced when the drug is administered. An important fact to remember is that the human body is composed only of cells, even though these cells are highly organized into tissues, organs, and systems. Consequently, all drugs produce effects by influencing the function of cells. Figure 1.1 shows the chemical structure of some common drugs.

Pharmacologists know that all drugs produce more than one effect. Every drug produces its intended effect, or **therapeutic effect,** along with several other effects. Drug effects other than the therapeutic effects are called **side effects.** Many side effects are more of a nuisance than they are harmful.

However, most drugs are capable of causing side effects that are potentially harmful. Such effects usually occur as the dose is increased or in patients who have particular health problems such as liver or kidney disease. When the side effects are particularly harmful or life-threatening, they are often called **toxic effects.** The appearance of toxic effects usually requires that the dose be reduced or the drug stopped.

TABLE 1.1 Major Areas of Pharmacology

Area	Description
Pharmacodynamics	Study of the action of drugs on living tissue
Pharmacokinetics	Study of the processes of drug absorption, distribution, metabolism, and excretion
Pharmacotherapeutics	Study of the use of drugs in treating disease
Posology	Study of the amount of drug that is required to produce therapeutic effects
Pharmacy	Science of preparing and dispensing medicines
Toxicology	Study of the harmful effects of drugs on living tissue

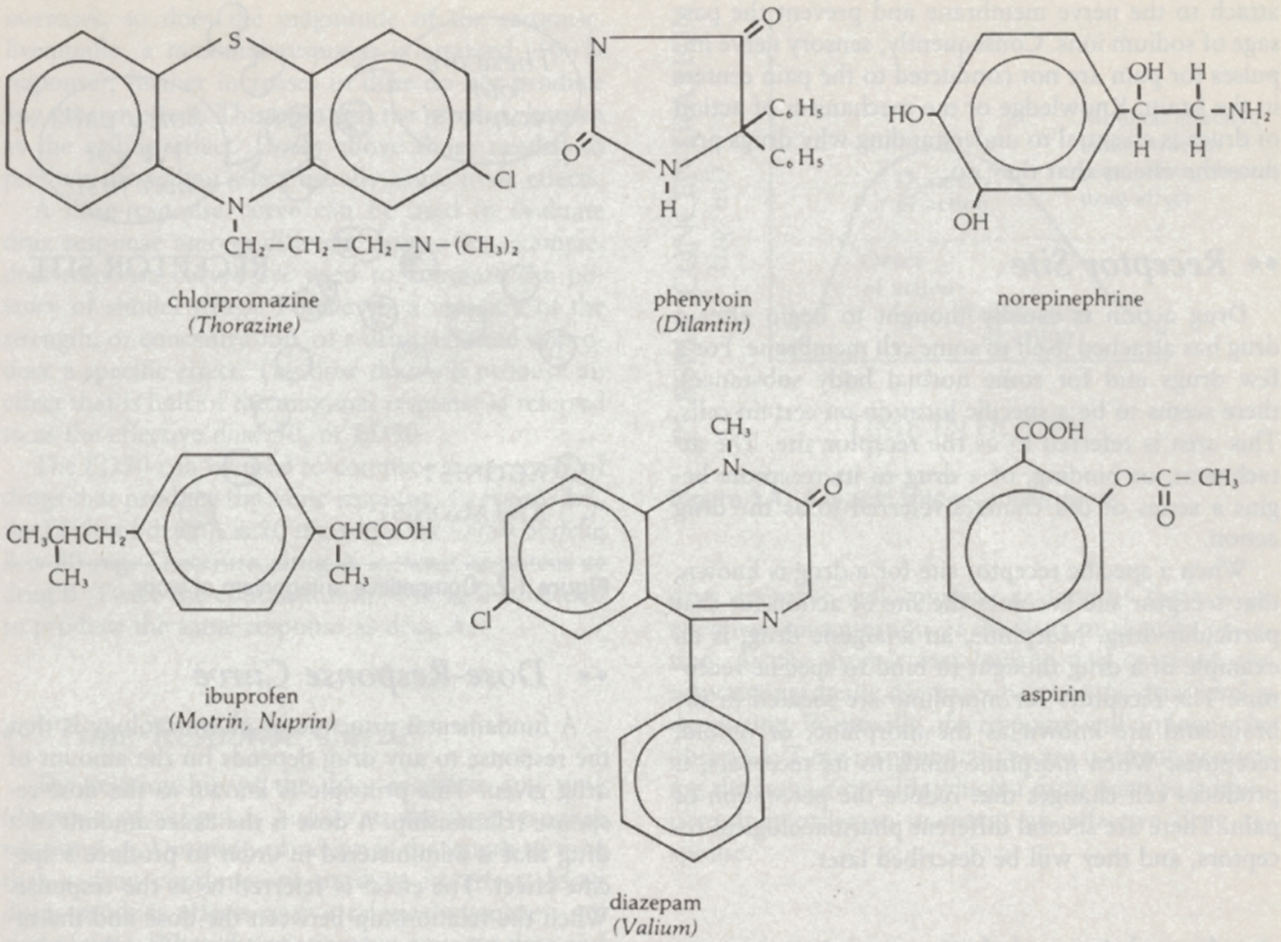


Figure 1.1. The chemical structures of several drugs.

Allied health personnel, especially nurses, spend the majority of their time in patient contact. Therefore, they have an important responsibility to recognize the side effects of drugs, particularly toxic effects.

BASIC CONCEPTS IN PHARMACOLOGY

As in any subject, fundamental principles and concepts form the basis upon which additional information can be added. Pharmacology is no exception, and the following basic concepts apply to any drug.

◆◆ *Site of Action*

The **site of action** of a drug is the location within the body where the drug exerts its therapeutic effect. The site of action of many drugs is not known. However, the site of action has been determined for a number of drugs. For example, the site of action of aspirin to reduce fever is in an area of the brain known as the hypothalamus. The hypothalamus normally regulates body temperature. Aspirin alters the activity of the hypothalamus so that body temperature is reduced. Throughout this book, when the site of drug action is known or suspected, it will be presented.

◆◆ *Mechanism of Action*

Mechanism of action explains how a drug produces its effects. For example, local anesthetic agents produce a loss of pain sensation by interrupting nerve conduction in sensory nerves. In order for nerve impulses to be conducted, sodium ions must pass

through the nerve membrane. Local anesthetic agents attach to the nerve membrane and prevent the passage of sodium ions. Consequently, sensory nerve impulses for pain are not conducted to the pain centers in the brain. Knowledge of the mechanism of action of drugs is essential to understanding why drugs produce the effects that they do.

◆◆ *Receptor Site*

Drug action is usually thought to begin after a drug has attached itself to some cell membrane. For a few drugs and for some normal body substances, there seems to be a specific location on certain cells. This area is referred to as the **receptor** site. The attachment, or binding, of a drug to its receptors begins a series of cell changes referred to as the drug action.

When a specific receptor site for a drug is known, that receptor site becomes the site of action for that particular drug. Morphine, an analgesic drug, is an example of a drug thought to bind to specific receptors. The receptors for morphine are located in the brain and are known as the morphine, or opioid, receptors. When morphine binds to its receptors, it produces cell changes that reduce the perception of pain. There are several different pharmacological receptors, and they will be described later.

◆◆ *Agonists and Antagonists*

Drugs that bind to specific receptors and produce a drug action are called **agonists.** Morphine is an example of an agonist. Drugs that bind to specific receptors but do not produce any drug action are called **antagonists.**

Antagonists are also known as blocking drugs. Usually, antagonists bind to the receptors and prevent other drugs or body substances from producing an effect. Naloxone, a morphine antagonist, is administered to prevent, or antagonize, the effects of morphine in cases of morphine overdose. There are many examples in pharmacology where drug antagonists are used to prevent other substances from exerting an effect.

When both agonist and antagonist drugs are administered together, they compete with each other for the same receptor site. This effect is known as competitive antagonism. The amount of drug action produced depends on which drug (agonist or antagonist) occupies the greatest number of receptors. The actions of a drug agonist and antagonist are illustrated in Figure 1.2.

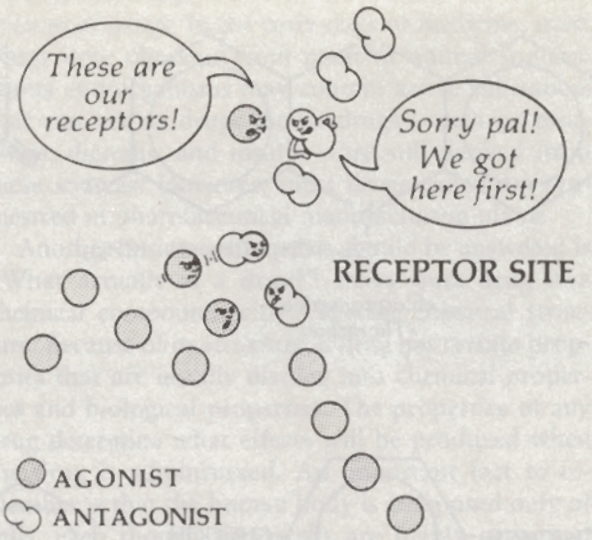


Figure 1.2. Competitive antagonism at work.

◆◆ *Dose-Response Curve*

A fundamental principle of pharmacology is that the response to any drug depends on the amount of drug given. This principle is known as the dose-response relationship. A **dose** is the exact amount of a drug that is administered in order to produce a specific effect. The effect is referred to as the response. When the relationship between the dose and the response is plotted as a graph, it is referred to as a dose-response curve.

Figure 1.3 illustrates the appearance of a typical dose-response curve for two similar drugs. The main feature of the dose-response relationship is that a

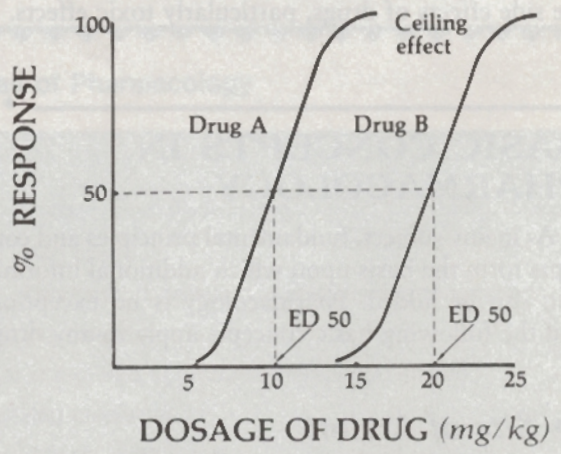


Figure 1.3. A typical dose-response curve.

drug response is proportional to the dose. As the dose increases, so does the magnitude of the response. Eventually, a maximal response is attained (100% response); further increases in dose do not produce any greater effect. This point on the graph is known as the ceiling effect. Doses above those needed to produce the ceiling effect usually cause toxic effects.

A dose-response curve can be used to evaluate drug response among different drugs. For example, dose-response curves are used to compare the potency of similar drugs. **Potency** is a measure of the strength, or concentration, of a drug required to produce a specific effect. The dose that will produce an effect that is half of the maximal response is referred to as the effective dose 50, or **ED50.**

The ED50 can be used to compare the potency of drugs that produce the same response. In Figure 1.3, the ED50 of drug A is 10 mg while the ED50 of drug B is 20 mg. Therefore, drug A is twice as potent as drug B. Twice the concentration of drug B is needed to produce the same response as drug A.

◆◆ *Time-Response Curve*

The relationship of the drug response and time (duration of action) is known as the time-response relationship. Duration of action is the length of time that a drug continues to produce its effect. Most drugs produce effects over a relatively constant period of time. When the relationship between time and response is plotted on a graph, it is known as a time-response curve. Figure 1.4 illustrates the appearance of a typical time-response curve. In this example, the drug response being measured is the plasma concentration of the drug. After drug administration, a certain amount of time is required before a drug will produce an observable effect.

The time from drug administration to the first observable effect is known as the onset of action. The drug response will continue as long as there is an effective concentration of the drug at the site of action. As the drug is metabolized and excreted, the response gradually decreases because the drug level is decreasing. Eventually, the response will no longer be observed. Time-response curves are used for predicting the frequency with which a drug must be administered in order to maintain an effective drug response.

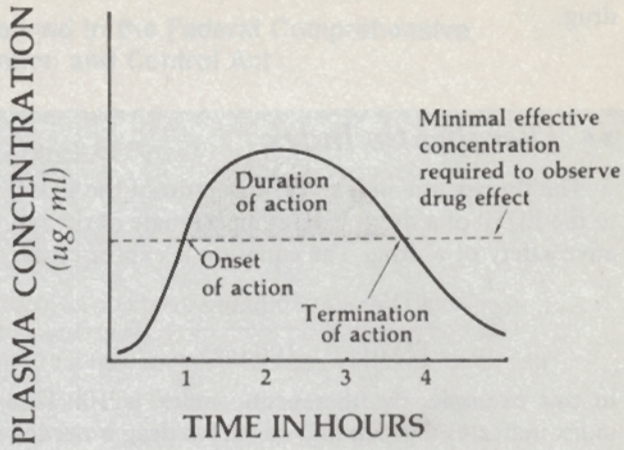


Figure 1.4. A typical time-response curve.

◆◆◆ Avoiding Toxicity ◆◆◆

All drugs will act as poisons if taken in excess. Only the dose separates a therapeutic effect from a toxic effect. The goal of drug therapy is to select a dose that is in the therapeutic range and avoid doses that produce toxicity. This task is not easy because many factors influence the amount of drug that reaches its site of action. These factors—such as route of administration, absorption, and drug metabolism—will be discussed in the next chapter.

DRUG SAFETY

The federal Food and Drug Administration (FDA) has established guidelines that govern the approval and use of all drugs. Every drug must fulfill two major requirements before it can be approved for use in humans: efficacy (proof of effectiveness) and safety. The drug must be effective in the disease state for which it has been approved. Approved drugs must satisfy specific safety criteria as determined by extensive animal testing and controlled human testing. As discussed, the dose separates therapeutic effects from toxic effects.

Drug safety receives much attention today. It is a constant source of concern and debate because the public is more aware of the dangers of drugs. In order to receive approval for use in humans, a drug must undergo several years of animal testing and evaluation. Several animal species must be used in order to evaluate the effectiveness and toxicity of a drug. One of the first tests that is performed is the lethal dose 50, or **LD50.** The LD50 is the dose that will kill 50% of the animals tested. The results of the LD50

and other tests are used to predict the safety of a drug.

Therapeutic Index

The **therapeutic index (TI)** is a ratio of the LD50 to the ED50 of a drug. It gives an estimate of the relative safety of a drug. The equation is expressed as:

$$TI = \frac{LD50}{ED50} = \frac{1000\ mg}{100\ mg} = 10$$

In this example, the therapeutic index is 10. This index indicates that ten times as much drug is needed to produce a lethal effect in 50% of the animals as is needed to produce the therapeutic effect in 50% of the animals. The therapeutic index is used only in animal studies to establish dosage levels for other testing procedures. The goal of drug therapy is to achieve therapeutic effects in all individuals without producing any harmful effects.

All drugs produce side effects and toxic effects if taken in excess. These unwanted effects are generally referred to as adverse effects. Most adverse effects are dose dependent, which means the higher the dose, the greater the chances for producing an adverse effect.

Certain tissues are more frequently affected than others. Oral drugs often cause nausea, vomiting, and diarrhea because of gastrointestinal (GI) irritation. The liver, kidneys, brain, and cardiovascular system may be adversely affected because these organs are exposed to the highest concentrations of the drug. Drugs that produce birth defects, such as thalidomide, are known as teratogens. Drugs that promote the growth of cancerous tumors are called carcinogens.

A few adverse effects are not dose dependent. These effects, such as drug idiosyncrasy and drug allergy, are determined by individual variation. Although all human beings are basically similar, there may be minor variations in certain enzymes or other body proteins. These variations may produce changes in drug metabolism that lead to unusual responses to a particular drug. An individual reaction to a drug with an unusual or unexpected response is known as an idiosyncrasy.

Drug allergy occurs when an individual becomes sensitized to a particular drug and produces antibodies against the drug (antigens). Subsequent administration of the drug leads to an antigen-antibody reaction. Antigen-antibody reactions involving drugs usually cause the release of histamine from cells known as mast cells. Histamine produces the characteristic symptoms of allergy, which include rashes, hives, itching, nasal secretion, hypotension, and bronchoconstriction.

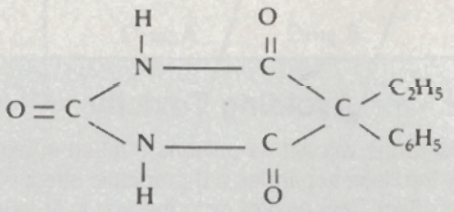
In serious allergic reactions, the symptoms may be so severe that death may occur. The term *anaphylaxis* is used to describe these serious allergic reactions.

DRUG NOMENCLATURE

All drugs are chemicals, and many have long **chemical names.** As a result, all drugs are given a shorter name, known as the nonproprietary name, which is usually a contraction of the chemical name. The nonproprietary name is more commonly referred to as the **generic name.**

When the drug is marketed by a pharmaceutical company, it is given a third name, known as the proprietary name, or **product name.** Since several different pharmaceutical companies may market the same generic drug, there may be several different product names for any one drug. Figure 1.5 gives three names of a commonly prescribed drug.

Drugs are also divided into prescription and nonprescription drugs. **Prescription drugs** require a written or phone order (the prescription), which can only be issued by a licensed physician. The prescription is a legal document that contains instructions for the pharmacist, who is licensed to dispense prescription medications. **Nonprescription drugs,** usually referred to as **"over-the-counter" (OTC) drugs** (such as aspirin, antacids, cold remedies), can be purchased anywhere and do not require the services of a physician or pharmacist.



Chemical name: 5,5, – phenylethylbarbituric acid
Nonproprietary name: phenobarbital
Proprietary names: LUMINAL, ESKABARB
(Trade name)

Figure 1.5. Drug nomenclature.

TABLE 1.2 Drug Schedules Defined in the Federal Comprehensive Drug Abuse Prevention and Control Act

Schedule	Definition	Controlled Drugs
Schedule I	Drugs with high abuse potential and no accepted medical use	Heroin, hallucinogens; these drugs are not to be prescribed
Schedule II	Drugs with high abuse potential and accepted medical use	Narcotics (morphine and pure codeine), cocaine, amphetamines, short-acting barbiturates; no refills without a new written prescription from the physician
Schedule III	Drugs with moderate abuse potential and accepted medical use	Moderate- and intermediate-acting barbiturates, glutethimide, preparations containing codeine plus another drug; prescription required, may be refilled 5 times in 6 months when authorized by the physician
Schedule IV	Drugs with low abuse potential and accepted medical use	Phenobarbital, chloral hydrate, antianxiety drugs *(Librium, Valium);* prescription required, may be refilled 5 times in 6 months when authorized by the physician
Schedule V	Drugs with low abuse potential and accepted medical use	Narcotic drugs used in limited quantities for antitussive and antidiarrheal purposes; drugs can be sold only by a registered pharmacist and the buyer must be 18 years old and show identification

◆◆ *Drug References*

Many reference books provide drug information. *The United States Pharmacopeia/National Formulary (USP/NF)* is the official drug list recognized by the U.S. government. It provides information concerning the physical and chemical properties of drugs. The *USP/NF* is revised every 5 years and is used primarily by drug manufacturers to ensure drug production according to official government standards.

The Physicians' Desk Reference (PDR®) is the reference most widely used by physicians, pharmacists, and nurses for information relating to the use of drugs in the practice of medicine. It provides information on indications for use, dosage and administration, contraindications, and adverse reactions. You should learn how to look up drugs in the *PDR®*.

◆◆ *Controlled Substances Act*

The Federal Comprehensive Drug Abuse Prevention and Control Act of 1970 is designed to regulate the dispensing of certain drugs that have the potential for abuse. These **controlled substances** are assigned to one of five schedules, depending on their medical usefulness and potential for abuse. Table 1.2 describes the schedules and provides examples of some controlled substances.

CHAPTER 1 REVIEW

Understanding Terminology

Match the definition in the left column with the appropriate term in the right column.

_____ 1. The study of the amount of drug that is required to produce therapeutic effects.

_____ 2. The study of the harmful effects of drugs on living tissue.

_____ 3. The study of the action of drugs on living tissue.

_____ 4. The study of drugs.

_____ 5. The science of preparing and dispensing medicines.

_____ 6. The study of the processes of drug absorption, distribution, metabolism, and excretion.

_____ 7. The study of the use of drugs in treating disease.

a. pharmacodynamics
b. pharmacokinetics
c. pharmacology
d. pharmacotherapeutics
e. posology
f. pharmacy
g. toxicology

Answer the following questions in the spaces provided.

8. Define a drug. _____

9. Differentiate between therapeutic effect, side effect, and toxic effect. _____

10. What is the difference between site of action and mechanism of action? _____

11. What is the relationship between ED50, LD50, and therapeutic index? _____

12. Explain the difference between a prescription drug, OTC drug, and a controlled substance.

13. Explain the difference between idiosyncrasy and drug allergy. _____

14. Write a short paragraph describing the terms: *receptor site, binding, drug action, agonist, antagonist,* and *competitive antagonism.*

Acquiring Knowledge

Answer the following questions in the spaces provided.

15. List three sources of drugs.

16. List three types of names given to drugs and define each.

17. What is a dose-response curve and what information is given by a dose-response curve?

18. What is the importance of a time-response curve?