PRACTICAL PHARMACOLOGY *for the* DENTAL HYGIENIST

STEVEN C. MONROTUS, B.A., D.M.D.

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STEVEN C. MONROTUS, B.A., D.M.D.

General Dental Practitioner;
Dental Staff, Deaconess Hospital,
Saint Louis, Missouri;
Dental Staff, Lutheran Medical Center,
Saint Louis, Missouri;
Instructor Dental Pharmacology,
Saint Louis Community College,
Saint Louis, Missouri.

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PREFACE

Since the turn of the last century the separate fields of medicine and dentistry have grown closer, and this trend has placed greater responsibility for treatment of the total patient on dental auxiliaries. Recent advances made in our understanding of the complexities of human function and treatment of disease require the expanded-function dental hygienist to prepare for this responsibility partially in the area of pharmacology. Ironically, the currently marketed textbooks of dental pharmacology for hygienists are either written or edited by researchers or periodontists who do not engage in general dental practice, do not assume the primary responsibility for delivery of dental care to the public, and do not represent a majority of the practitioners who could engage the services of a hygienist. While such textbooks are excellent works for the authors' peers, they obviously fall short of providing students a level of instruction that would prepare them to adequately manage clinical situations involving drugs and drug-related techniques encountered in a general dental practice; the difficulty students have extracting pertinent information from such references has been repeatedly demonstrated by the low scores generally seen in this area on the National Board Examination.

The dental hygienist is a clinician, not a researcher. Although theoretical aspects have been included here to clarify matters of clinical importance, no attempt has been made to improve on the many theoretical works available. An exhaustive presentation has been abandoned in favor of providing a clinically relevant base from which subsequent study may be made as the hygiene student learns to assimilate and recall details in a way analogous to that of the dental student. The design of this approach has been to produce another well-informed clinician who can interact harmoniously with the general dentist or dental specialist as dental diagnostic problems are tackled every day and solved.

The focus of this book was not on producing another typical tour de force on drugs but on serving the dual purpose of aiding the student during instruction on a rigorous subject and in passing the National Board Examination, and on training the graduate hygienist whose background in this area may be weak or poorly correlated with practice. To limit the textbook to a manageable size for classroom use, space was not wasted on definitions of terms found in medical dictionaries or on explanations of certain basic concepts of mathematics, chemistry, anatomy, or physiology unless the material was critically important. Students unfamiliar with such terms or concepts are referred to standard references for further information.

Curriculum Essentials for Dental Hygiene Education, published by the American

Dental Hygienist's Association, was used as a guide for content, and topics were organized for incorporation into a sixteen-week semester allowing time for examinations. The order of presentation of topics has been based on results of actual classroom testing, in which higher examination scores were made using the present format. New material is based only on previous material or pertinent material within the chapter and is cross-referenced. As the need arises, the beginning student is given more than one exposure to certain basic and critical information.

Certain related topics in the areas of nutrition, dental public health, patient evaluation, medical emergencies, and dental surgery and anesthesia were included in this book in the interests of completeness. Since the mechanism of action of the autonomic drugs is theoretical, the cardiovascular agents were presented ahead of them to emphasize the fact that many drugs with cardiovascular or pulmonary effects exert these effects outside the realm of autonomic receptor theory. The choices of morphine, nalorphine, and aspirin were arbitrarily made as standards of comparison to assess relative potency of similar drugs, but other analgesics could also have been used. A separate generic drug index was prepared to encourage learning of generic rather than trade names and to assist in reviewing for examinations.

Special thanks are given to Dr. Ira Shannon for his cooperation with the section on fluorides, to Paul D. Nelson for his years of encouragement, proofreading, and preparing the illustrations and indexes, and to the editors for their patience and suggestions. The students at St. Louis Community College deserve special mention for displaying an interest that became the inspiration for this textbook and without which the project would never have been begun and completed.

S. C. Monrotus, B.A., D.M.D.
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GENERAL PHARMACOLOGY

SECTION 1: GENERAL PRINCIPLES OF DRUG ACTION

Drug-Related Fields

There are no sharp lines of demarcation separating the various drug-related fields, but the following are useful definitions:

Pharmacology – the study of drugs.

Pharmacy – the science dealing with the procurement, preparation, and dispensing of drugs.

Pharmacodynamics – the science dealing with the mode of action and with the metabolism of drugs.

Pharmacotherapeutics – the science dealing with the use of drugs in the treatment of disease.
Pharmacognosy – the science dealing with the identification of naturally occurring drugs.
Posology – the study of drug dosage.
Toxicology – the study of poisons.

A drug is loosely defined as any chemical substance capable of affecting a biological system. Over 7500 such drugs affecting man have been described, and about 325 (4.3 per cent) of these are clinically important to the dental hygienist.

Periodic Literature

There are several sources for obtaining information on drugs and their uses.

The **United States Pharmacopeia** (USP) is issued every five years and it sets manufacturing standards related to strength and purity. The initials USP on a bottle label following the name of a drug insure that it has been manufactured with the greatest care.

The **British Pharmacopeia** (BP) is the English equivalent of the USP and is official in Canada and Great Britain.

The **National Formulary** (NF) is issued every five years and describes standards for drugs that are widely used or that have high therapeutic value.

The **AMA Drug Evaluations** (ADE) contains information on drugs introduced in the United States during the preceding ten years and on all drugs in current medical use.

The **Physician's Desk Reference** (PDR) is issued every year by some 200 drug manufacturers and contains product descriptions and a product identification section showing about 1300 tablets and capsules in full color and at actual size for easy comparison. It does not describe all drugs currently in use, but it is cross-indexed to include generic and trade names, and it describes about 2500 drug products.

Accepted Dental Therapeutics (ADT) is issued every two years by the **Council on Dental Therapeutics** of the ADA. It is designed to assist the dental practitioner in the selection of drugs for treatment of oral disease.

Facts and Comparisons (FC) is a loose-leaf listing of over 6000 drugs in current use, and it summarizes pertinent prescribing information. It is continuously updated with monthly supplements and is the most complete and up-to-date source available for rapid reference in a dental office. No dental office should be without one.

Drug Nomenclature

The **naming of drugs** becomes confusing to the student because the same drug may have several names.

The **chemical name** of a drug conveys the chemical structure and is first used when the drug is tested experimentally.

When the drug is found to be therapeutically useful the **United States Adopted Name Council** (USAN) gives it a generic name that will not conflict with other drug names. The company marketing the drug also gives the drug a **trade name** (proprietary name) which is, for promotional purposes, generally short and easy to remember.

Because the generic name is the official name of a drug and is the one used in the

USP and NF, it is preferred over the trade name(s). When the generic name of a drug is learned, it is unnecessary to learn a large number of trade names.

To illustrate the various names of a single drug we will use lidocaine as an example:

Chemical name:	2-diethyl-amino-2′6′,-aceto-xylidide
Genelic name:	lidocaine
Trade names:	Xylocaine
	Octocaine
	Doricaine
	ProLido

In all subsequent discussions we will use the generic name followed by a common trade name in parentheses, for example, lidocaine (Xylocaine).

Routes of Administration

The following are the various avenues by which drugs may be introduced into the human body:

1. **Enteral Routes**

   a. **Oral Route.** The simplest way to introduce a drug into the body is by mouth, and this is the method most often used.

   Advantages: Absorbing area of the intestine is large.

   Patients are usually cooperative.

   In overdosage most of drug can be retrieved by pumping the stomach.

   Disadvantages: Some drugs are deactivated by hepatic-portal circulation.

   Blood levels are less predictable.

   Onset is delayed by slower absorption.

   Gastric irritation is possible and may result in nausea.

   b. **Rectal Route.** Drug suppositories are often placed in the rectum when the oral route is impractical or impossible.

   Advantages: Patient cooperation is unnecessary.

   The GI tract is not irritated.

   Administration is not prevented by nausea or unconsciousness.

   Disadvantages: Absorption is decreased compared to that of upper intestine.

   Absorption is irregular and incomplete.

2. **Parenteral Routes**

   a. **Intravenous Route (I.V.).** Drugs may be given through the superficial veins of the forearm, the dorsal veins of the hand, or the veins of the ankle.

Advantages: It is the most rapid method of eliciting a drug response.

The drug response is the most predictable.

Constant plasma levels are most easily obtained by this method.

This route accommodates the largest volume of drug solution.

Disadvantages: Drug injected cannot be retrieved.

Rapid injection produces undesirable effects.

Needle trauma may result in bruising.

Conscious patient is placed under stress.

b. **Intramuscular Route (I.M.).** Drugs may be given by injection into muscle, such as the deltoid, the lateral head of the triceps, or the gluteus medius.

Advantages: Absorption is rapid (anterior quadriceps absorbs most rapidly and is often used for hypodermoclysis).

Irritating drugs are well tolerated.

Large amounts of solution can be accommodated.

Disadvantages: Repetitive drug administration is inconvenient.

Conscious patient is placed under stress.

c. **Subcutaneous Route (Sub-Q).** Drugs may be injected below the dermis of the skin.

Advantages: Absorption is slow, a requirement for certain drugs, such as insulin.

Rate of absorption can be controlled with ice packs or topical epinephrine.

Disadvantages: Irritating drugs result in painful injection in conscious patient (conscious patient is placed under stress).

Only a small amount of drug solution is accommodated.

Other less frequently used parenteral routes are:

d. **Intradermal Route.** Drugs may be injected into the dermis of the skin (usually small amounts of local anesthetic are injected first, after which longer needles may be passed painlessly for deeper injections).

e. **Intrathecal Route.** Drugs may be injected into the spinal subarachnoid space (usually drugs needed to treat certain infections of the meginges).

f. **Intraperitoneal Route.** Drugs may be injected into the peritoneal cavity and absorbed via the mesenteric veins. This route has fallen into disuse because of the hazards of infection and adhesions.

g. **Inhalation Route.** Drugs in solution can be atomized and the aerosols can be inhaled, with absorption occurring via the mucous membranes of the respiratory tract. This route is often used when the agents are volatile or gaseous.

h. Topical Route. Drugs in solution may be applied anywhere on the skin or at epithelial surfaces of the eye, ear, nose, vagina, or urethra. This route is often used in the oral cavity for treatment of certain infections and administration of topical anesthetics.

Factors Influencing Drug Absorption

There are several factors that influence the rapidity and degree of absorption of drugs into the body.

Route of Administration. By far the most important factor is the route of administration. In general the parenteral routes offer more rapid and complete absorption than do the enteral routes.

Physical State. The **physical state** in which the drug is administered will also affect its absorption. In general, drugs in solution are more rapidly and completely absorbed than are drugs in tablet or capsule form.

Solubility. The **solubility** of a drug will also affect its rate of absorption. In general, water-soluble drugs are more rapidly and completely absorbed than are those that are fat-soluble.

Concentration. The **concentration** of the drug presented to the absorbing surface will affect its absorption. In general, food or water taken before, with, or after a drug is administered orally will decrease the amount of drug absorbed and the rate of absorption. Drugs given parenterally in high concentration may result in chemical irritation with reduced absorption.

Drug Diffusion and Transportation

In order for drugs to exert their effects after administration they must first traverse cell membranes. The **cell membrane** has been described as a lipid bilayer covered on both sides by protein, and it is approximately 100 angstroms wide (1 **angstrom** = 10^{-10} meter). Special openings in the membrane called **pores** are scattered randomly on its surface, and are about 8 angstroms wide, except for **capillary pores**, which are about 30 angstroms wide. The pores are lined with positive charges and are capable of regulating the passage of small molecules and ions in and out of the cell. Drugs with molecular weights of 200 or less may pass through all membrane pores, but drugs with molecular weights *as high as* 60,000 may pass through capillary pores. This process is known as **filtration.**

Extensions of the lipid bilayer also protrude through the protein covering of most membranes to the surface and in an unknown way enable lipid-soluble substances to move across the lipoprotein membrane by the process of **simple diffusion** from an area of higher concentration to an area of lower concentration. The amount of drug that diffuses is proportional to its **lipid solubility** and the concentration gradient. Therefore, whenever a drug is present outside a cell, the cell membrane becomes a barrier that exhibits a selective permeability depending on the drug's molecular size, valence (charge), and lipid solubility.

The passage of certain substances, such as glucose, across membranes is mediated by specific carrier substances within the membranes that are as yet unidentified. A drug bound to a carrier substance may pass through a membrane and be released on the other side of the membrane along its own concentration gradient by the process known as **facilitated diffusion.**

Specialized cells, such as those of nerves and muscle, are capable of transporting a substance through their membranes against an electrochemical or concentration gradient, a process which is termed **active transport**. This requires an energy expenditure, and more energy is needed to actively transport a charged particle than a neutral one.

When drugs enter the plasma they commonly undergo a reversible binding to a high molecular weight protein, **albumin**. Since only the unbound portion of the drug is active, the bound portion does not contribute to the intensity of drug action. The bound and unbound forms are in equilibrium with each other, and as more of the unbound form is used the equilibrium shifts to release more of the bound form from storage, and drug activity is prolonged. Standard doses of drugs that are highly bound may become toxic when followed by drugs that displace them from their binding sites on plasma albumin.

If all the albumin binding sites have been occupied, a drug may begin to saturate the globulin fraction of plasma as well. Certain drugs may undergo initial binding to the globulins rather than to albumin.

Sites of Drug Elimination

Drugs are removed from the body at certain sites which are classified as either major or minor in importance:

MAJOR SITES

Liver. The liver is the prime organ of drug detoxification and elimination and concentrates unmetabolized drugs and their altered metabolites in the bile or metabolizes and degrades drugs in the circulation for eventual removal by the kidney. Drugs eliminated in the bile are stored in the gall bladder and during reflex stimulation are deposited into the lumen of the small intestine, where they are eventually removed in the feces by the colon.

Kidney. The rate and extent of excretion of drugs in the urine depends upon glomerular filtration and tubular secretion acting to remove drugs from plasma and eliminate them in the urine and upon active and passive tubular reabsorption, which transports some of the filtered substances back into the plasma.

Colon. The colon eliminates drugs that are not completely absorbed after oral administration and those that are not well absorbed after biliary excretion. Drugs excreted in bile that are reabsorbed by the intestines find their way back to all other sites of elimination.

Lung. The rates of elimination of gaseous end products of metabolism depend on the partial pressures of gases in the inspired air, alveolar air, and pulmonary capillaries, the solubility of the drug in plasma, the blood flow in the tissues, and the presence of other gases.

MINOR SITES

Mammary Gland. Unless proven otherwise any drug taken by a pregnant woman should be expected to appear in the breast milk. Women receiving medication during their pregnancies should be advised not to nurse their children.

Sweat Gland. Certain drugs may appear in perspiration shortly after administration.

Lacrimal Gland. Drugs excreted into tears may be discharged to the external environment or swallowed and ultimately removed by the kidney or colon.

Salivary Gland. Drugs excreted into saliva are largely swallowed and also ultimately removed by the kidney or colon.

Non-Glandular Structures (Placenta, Epidermal Structures, and Teeth). To the extent that the fetus is a drug depot apart from the mother the placenta is considered an excretory organ for drug elimination. Slow removal of minute quantities of drugs is also possible in shed epidermis, trimmed hair and nails, and extracted teeth.

Categories of Group Drug Actions

Drugs can modify the action of cells by (1) initiating a cellular response, causing cells to produce certain materials; (2) stimulating or depressing cellular activity, causing cells to increase or decrease their functions; (3) changing the usual effect of another drug on cells, producing a different response to the drug or no response at all; and (4) exerting purely physical or chemical effects.

A **drug receptor** is a specialized cellular or tissue element with which a drug interacts to produce its biological effects; it is believed that receptors are macromolecules (proteins, lipoproteins, enzymes, or nucleic acids) that form a complex with a drug to trigger a series of chemical events. Such receptors are theoretical constructs that help to explain experimental observations and have not been demonstrated histologically; they are postulated to exist solely to explain the action of certain drugs whose actions cannot be explained otherwise, such as antihistamines (histamine H_1 and H_2 receptors), phenothiazine tranquilizers (dopamine receptors), and autonomic drugs (cholinergic and adrenergic receptors) (Chap. 5, Sec. 4; Chap. 6, Sec. 2; Chap. 7, Sec. 2). The series of chemical events triggered by the above receptors, as well as by many of the hormones (Chap. 4, Sec. 1) appears to involve the activation or inhibition of the cellular enzyme adenyl cyclase, which in turn changes the levels of cyclic AMP (adenosine monophosphate) within the target cell.

Affinity is the ability of a drug to combine with a receptor, whereas **efficacy** is the ability of a drug to induce a response subsequent to occupation of the receptor. An **agonist** is a drug that exhibits an affinity with a receptor such that combination of the drug and the receptor produces a functional change in the surrounding tissue; an **antagonist** is a drug that exhibits zero efficacy at a given receptor. Agonists therefore possess both receptor affinity and efficacy. Antagonists have affinity but lack efficacy.

Effects of Multiple Drug Administration

Whenever two different drugs are introduced into the body simultaneously they will either (1) enhance each other, (2) antagonize each other, or (3) have no effect on each other.

Enhancement of effect may come about through (1) **addition,** whereby the effect of single doses of two drugs acting in the same direction is greater than that expected for one of the drugs acting alone; (2) **summation,** whereby the combined effect of single doses of two drugs acting in the same direction is exactly equal to the algebraic sum of the individual responses; (3) **synergism,** whereby the effect of single doses of each of two drugs is greater than the algebraic sum of the individual effect when each drug is administered alone; and (4) **potentiation,** whereby the administration of a drug with no effect

on a given receptor causes an exaggerated response to the administration of another drug. In some instances potentiation is used as a synonym for synergism and is broad in its meaning.

Antagonism may take the form of (1) physiological antagonism, whereby two drugs acting normally may oppose each other by acting in opposite directions; (2) chemical antagonism, whereby an active drug combines chemically with another, its antagonist, to form a compound with either no activity or less activity than the original drug; and (3) specific antagonism (competitive inhibition), whereby a drug interferes with the combination of another drug with a response system through competition for receptor sites for which both agents have a particular affinity.

No drug is so precisely specific for receptors in all patients that it is effective in exactly the desired manner, nor is any absolutely free of producing unsought reactions in some patients. Therapeutic effects primarily sought are desired drug actions, whereas additional effects not primarily sought are termed **drug reactions**, or adverse drug actions.

Whenever several drugs are administered to a patient concurrently the incidence of drug reactions increases as the number of drugs taken increases. Table 1–1 illustrates drug reaction frequency as a function of the number of drugs administered at one time.

Drug Susceptibility

Patients responding to substandard doses of a drug are considered to be **hypersusceptible** to that drug and all other chemically similar drugs. In practice, these patients are usually identified as those who complain of having a system that is sensitive to medicine of any kind and who usually refuse drug therapy.

Patients responding only to suprastandard doses of a drug are considered to be **hyposusceptible** to that drug and all other chemically similar drugs. In practice, these patients are usually identified as those who claim to have a system that is resistant to most medicine and who are usually reluctant to comply with drug therapy.

When patients are hyper- or hyposusceptible to certain drugs, they often extend their feelings of apprehension to drug therapy of any kind, including local anesthesia for root planing. Such patients would rather suffer quietly during a subgingival debridement than allow the operator to administer a dental injection to relieve their discomfort. In such cases it is best not to force treatment on a patient and in a friendly confident way complete the dental prophylaxis with respect for the patient's wishes.

Factors Affecting Patient Response

There are several factors that can affect response to drug administration:

Table 1–1. DRUG REACTION FREQUENCY*

Number of Drugs Administered	*Reaction Rate*
5	4.2%
6–10	7.4%
11–15	24.2%
16–20	40.0%
21 or more	45.0%

*From Martin, E. W., Hazards of Medication, 2nd ed., J. B. Lippincott, 1978, reprinted with permission.

Variations in Animal Species. In veterinary science qualitative and quantitative differences in the response of animals to different drugs are observed. Certain drugs producing a given effect in certain animals may have the opposite effect in man or may require dosage changes based on mg/kg body weight.

Age of Patient. Standard adult doses of drugs assume that the dose is administered to a patient between 12 and 60 years of age. Infants, children, and geriatric patients require reduced doses because children have a smaller body surface area and hence a smaller body mass for drug distribution, and the elderly have a reduced metabolic rate and fail to degrade and eliminate drugs as rapidly as younger people.

Presence of Other Drugs. Although some drug combinations produce no interactions whatsoever, antagonism or enhancement of effect may occur and produce respectively no response to a given drug or an exaggerated response.

Body Temperature. Elevated body temperature in febrile states may alter the rate at which a drug is metabolized by increasing the metabolic rate, and high blood levels of a drug are more difficult to maintain over several hours. Control of high fever in infants, for example, often requires more than one antipyretic drug administered simultaneously.

Presence of Disease. Certain drugs will exert their therapeutic effects only in the presence of disease and will cause no response in the normal patient. Antipyretic drugs, for example, have no effect on normal body temperature.

Certain diseases may also affect drug susceptibility. Hyperthyroid patients, for example, are unusually sensitive to epinephrine.

Time of Administration. Some drugs are poorly absorbed when taken orally at mealtime and may require that the patient take them between meals in order to obtain the proper blood levels of the drug.

The Placebo Effect. Placebos ("sugar pills") are inert substances whose value lies in their function as symbols of the doctor's healing power. Doctors themselves are capable of affecting a patient's response by transmitting to the patient their knowledge of the potency of the drug. The positive therapeutic response of a patient to an inert substance prescribed by a doctor is called "the placebo effect" and has been shown to be a powerful tool.

The strength of the placebo effect increases with that of the medication to which it is compared. In double-blind experiments on pain relief, placebos have been reported to be 55 per cent as effective as both mild and strong analgesics. Other studies suggest that at least 50 per cent of the short-term effect of any drug that affects subjective states (pain, anxiety, and so forth) are attributable to the placebo effect.

States of mind may affect the course of cancer in some patients, and spectacular remissions in response to the administration of a placebo have been reported by several investigators. This is believed to be the result of developing in the patient's mind a very strong anticipation of cure. Such treatment, often called the "psychological approach" should be considered only in patients who are willing to expend considerable effort and to endure psychic pain, in patients who are surgically inoperable, in patients who no longer respond to radiation, and in patients for whom conventional chemotherapy is contraindicated. With these limitations in mind, the psychological approach to cancer treatment is necessarily very restricted and should be viewed only as a last resort.

Age of Prescription (Stability of Drug Preparation). Medicine of any kind that was prescribed prior to the current illness or for someone else should be disposed of by flushing down a toilet. There are many drugs that will cause patients to become violently ill if taken after their shelf-life has expired, such as minocycline (Minocin) (Chap. 2).

Different salts of the same drug may be more or less stable in solution due to decreased or increased water solubility, with resulting changes in potency as the time from manufacturing increases, as occurs with propoxyphene (Chap. 8, Sec. 2).

Dose Response Curve and Therapeutic Index

The first step in evaluating the toxicity of any drug before it is marketed is to determine its lethality in experimental animals. A large number of animals are given a test dose of the drug, and the number of deaths is plotted as a function of the dose administered. When this is done a sigmoid (S-shaped) curve is obtained, and the **lethal dose** required to kill 50 per cent of the animals so treated is defined as the LD_{50} and is expressed in units of mg/kg body weight.

In a similar way the **effective dose** required to elicit the desired response in 50 per cent of the animals tested is defined as the ED_{50} and is always less than LD_{50}.

Since all drugs are toxic at some dose, the LD_{50} is meaningless unless the ED_{50} is also known. The ratio of LD_{50}:ED_{50} is known as the therapeutic ratio, or therapeutic index of the drug. The higher the therapeutic index (TI) of a drug, the less chance there will be of a toxic reaction upon its administration and the greater its use in therapy. (See Fig. 1–1.)

SECTION 2: ADVERSE DRUG ACTIONS

Untoward Reactions

Untoward, or undesirable reactions to drugs may take place in the body in addition to the desired responses.

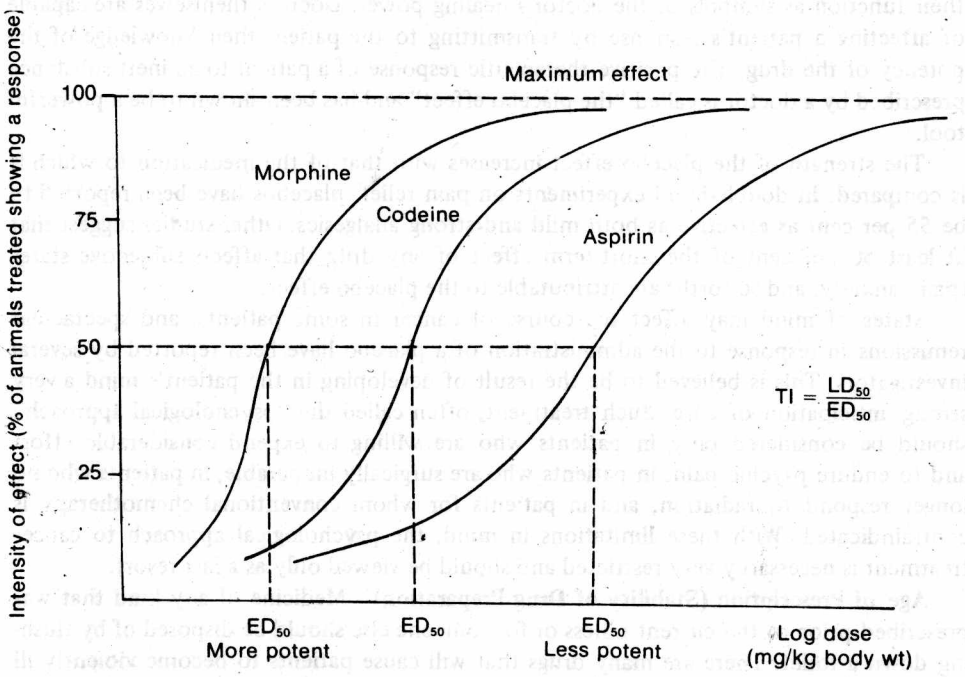

Figure 1–1. Dose response curves of three analgesic drugs comparing dosage and effectiveness.