Lippincott Williams & Wilkins'

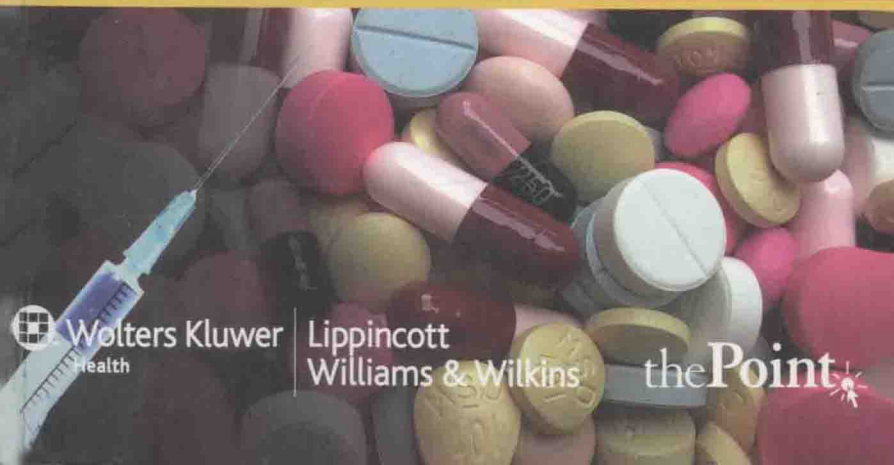
Dental Drug Reference

with Clinical Implications

CD-ROM with Printable Drug Monograph

Second Edition

Frieda Atherton Pickett, RDH, MS
Géza T. Terézhalmy, DDS, MA



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Lippincott Williams & Wilkins' Dental Drug Reference with Clinical Implications Second Edition

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Preface

The second edition of *Lippincott Williams and Wilkins' Dental Drug Reference with Clinical Implications* is designed as a quick and concise pharmaceutical resource for dental professionals. This unique reference has been updated to deliver clinically relevant information to be used chairside during the review of a patient's medical history. In addition to providing data on the drugs encountered and used in dentistry, *LWW's Dental Drug Reference with Clinical Implication, Second Edition*, also serves as an up-to-date reference for the pharmacological management of orodental pain, oral infections, and common mucocutaneous conditions, and also presents a practical approach to relevant adverse drug events.

The text begins with a discussion of general principles of pharmacology and adverse drug events, an understanding of which is essential for the rational use of drugs in the prevention, diagnosis, and treatment of disease. Subsequent chapters provide insightful information related to the risk stratification and dental management of the patient taking medication for a variety of systemic diseases, concise information relevant to the management of odontogenic pain and infection, and a common sense approach to the potential medical emergencies one may encounter in the oral health care setting. Prescription examples can be found in the section on the medical management of selected oral conditions. Full-color clinical photographs of common mucocutaneous conditions and oral manifestations of adverse drug effects are included in an image insert at the back of the book.

The attached CD-ROM contains all of the drug monographs in a fully searchable format; drug monographs may also be printed and placed in the patient's chart.

Readers may receive continuing education credits for the personal study of the Clinical Medicine and Therapeutics chapters in Section 1. Refer to p. ii at the front of the text for additional details.

The A to Z Listing of Drugs provides information relevant to dentistry on over 3,700 trade and generic drugs. We have made every effort to include current, up-to-date information as it was available at the time of manuscript preparation. However, the user should be cautioned that therapeutic recommendations change as new drugs and new drug information becomes available.

The appendices present information that is not readily available in other reference sources but which may be helpful to the oral health care provider. This includes a Spanish-English translation guide, a list of herbal and nutritional supplements and how they may effect dental care, and product-specific information such as toothpastes that do not contain sodium laurel sulfate.

Our goal in revising *LWW's Dental Drug Reference with Clinical Implications*, was to provide relevant, concise information in a conveniently-sized book that can be stored in the dental operatory. Our focus was to include drugs likely to be reported on the health history and drugs that the dental professional would be likely to use. For that reason, not all drugs are included. If the user encounters a drug that has not been included, but should be, you are asked to notify Lippincott Williams & Wilkins via e-mail to DDR@LWW.com.

Frieda Atherton Pickett, RDH, MS
Géza T. Terézhalmy, DDS, MA

How To Use This Book

Lippincott Williams and Wilkins' Dental Drug Reference with Clinical Implications is divided into three sections.

Section 1: Clinical Medicine and Therapeutics may be read at one's convenience or may be referred to during the clinical decision-making process. The chapters on General Principles of Pharmacology and Adverse Drug Events (the latter of which includes corresponding clinical photographs at the back of this book) provide crucial information on prescribing or using drugs in the clinical setting, and on how other drugs the patient may be taking will affect their oral care. Chapters 3 and 4 describe current recommendations for Medical Management of Pain and Medical Management of Odontogenic Infections. The chapter on the Medical Management of Selected Oral Conditions includes sample prescriptions and corresponding clinical images at the back of the book. The first section of the book is rounded out with a chapter on Clinical Medicine, with recommendations for the dental management of patients with selected systemic diseases, and a chapter outlining a stepwise approach to the Management of Medical Emergencies in the Oral Health Care Setting. The University of Texas Health Science Center at San Antonio, Dental School, is offering Continuing Education credits based on these seven chapters. Instructions on how to obtain CE credits can be found on p. ii at the front of the text.

Section 2: A to Z Listing of Drugs includes concise, clinically relevant dental information for individual drugs or drug combination products likely to be reported on the health history, along with expanded information on drugs prescribed by the dentist. Drugs are listed alphabetically by generic name; brand names and synonyms are cross-referenced to the appropriate generic drug name in the Index. The *concise drug monographs* present information relevant to the oral health care treatment plan. *Drugs likely to be prescribed or used by the dental professional* are identified by a tooth icon (🦷) next to the generic name and contain expanded information to include dosages for the various forms of the product (topical, oral, injectable), interactions, pharmacokinetics, clinical indications, and the pregnancy risk category of the drug.

The following outlines the points of information that are included in each drug monograph. Information that is listed only for drugs prescribed or used by the dental professional are indicated by the tooth icon (🦷).

GENERAL INFORMATION

Drug Name

The generic drug name is listed at the top of each drug monograph, followed by the phonetic pronunciation in parentheses. The pronunciations are based on the USAN Council officially designated pronunciations. If there are alternate generic names used for a particular drug, they will appear in small black font after the written pronunciation, enclosed in parentheses. Common synonyms are preceded by the title "Synonyms."

Trade Name

U.S. trade names for each drug are listed in bold black font. If the drug is administered or prescribed by a dental care provider, the available dosage forms and dosages follow the trade drug name. Common Canadian trade names are indicated by the Canadian flag icon (🍁). Common Mexican trade names are preceded by the Mexican flag icon (🇲🇽). If a trade name is available in both the

U.S. and Canada or Mexico, it will appear in the U.S. list only.

Drug Class — The drug class indicates the drug's classification or therapeutic category.

DEA Schedule — If a drug is a controlled substance, the U.S. Drug Enforcement Administration schedule is listed.

PHARMACOLOGY

Action — Action describes how the drug works.

Uses — All approved indications for the drug are provided.

Unlabeled Uses — Unlabeled uses (indications for which the drug is frequently used but for which it is not approved) are given when applicable.

Contraindications — Contraindications are listed when appropriate. Hypersensitivity to a given drug is always a contraindication and, therefore, this fact is assumed and has not been repeated for every monograph. *Standard Considerations* appears when there are no specific contraindications other than hypersensitivity.

Usual Dosage — The route of administration and typical dosages are provided. Where applicable, dosages are organized by age group and/or condition.

Pharmacokinetics — The Pharmacokinetics section details the absorption (ASORP), distribution (DIST), metabolism (METAB), excretion rate (EXCRET), onset, peak, and duration of the drug, along with useful information on how pharmacokinetic factors differ in certain populations (SPECIAL POP).

Drug Interactions — Drug interaction information indicates the drug category or specific dental drug likely to interact with the subject drug, the likely mechanism of the interaction, and the clinical dental recommendation for the interaction. For *concise drug monographs*, only drug interactions that are relevant to dental treatment are listed, under the heading Drug Interactions Related to Dental Therapeutics. For *drugs that are likely to be used or prescribed by a dental professional*, a more comprehensive listing of interactions is provided. Drug interaction information included throughout the drug monographs is based primarily on clinical reports, with some theoretical interactions. Since new drug interactions are being reported daily, it is important to note that the absence of information doesn't always imply safety.

Adverse Effects — Common or life-threatening adverse reactions for the drug are listed according to the following body systems: oral, central nervous system (CNS), cardiovascular system (CVS), gastrointestinal system (GI), and respiratory system (RESP). Other applicable adverse reactions are listed after the miscellaneous (MISC) heading.

CLINICAL IMPLICATIONS

General — The General section addresses the clinical implications of the drug effects or of the medical condition for which the drug is prescribed. The information provided here may reflect potential changes to the treatment plan and should be reviewed thoroughly prior to initiation of treatment. Where applicable, information is separated into "When prescribed by the dentist" and "When prescribed by medical facility."

Pregnancy Risk Category — Indicates the FDA pregnancy risk category for the drug.

Oral Health Education — The section on Oral Health Education lists information that should be shared with the patient or caregiver, including information on the drug's administration, potential side effects, and safety precautions.

Section 3: Appendices provide clinically useful information in an easy-to-use format. Drugs Listed by Therapeutic Category or Condition can be referenced when the patient cannot recall the name of a drug being taken. Locate the category the agent would most likely fall under, such as "antihypertensive agents," and have the patient look through the list of drug names to identify the drug being used. The Abbreviations appendix defines the abbreviations and acronyms used throughout the drug monographs. Herbal and Nutritional Supplements of Interest to Dentistry lists dentally-relevant information for supplements likely to be consumed. This list is not all-inclusive, and suggestions for updates or additions can be submitted to LWW via e-mail to DDR@LWW.com. Spanish/English Dental Communication Guidelines covers common phrases to assist the dental professional when communicating with a Spanish-speaking patient. The appendix on In-Office Preventive Products is comprised of specific information on products in various categories, including: fluoride varnishes; toothpastes without sodium laurel sulfate, cinnamon or methylparaben; products with therapeutic levels of xylitol; and oral rinses without alcohol. The Laboratory Values for Normal Limits appendix addresses normal values as well as safe limit values for the most common laboratory tests the dental professional would consider when completing a medical consultation.

All of the drug monographs in this handbook are included on the CD-ROM in an easy-to-use, searchable format. Drug information can be printed from the CD and placed into a patient's record for quick reference.

The inside front cover of the text summarizes guidelines for antibiotic prophylaxis prior to dental procedures in specific population groups. The American Heart Association guidelines to prevent bacterial endocarditis following specific oral procedures can be found on the inside front cover of the book; the American Dental Association/American Academy of Orthopedic Society guidelines for total joint removal (TJR) situations are printed opposite the AHA guidelines.

Acknowledgements

The authors wish to express their sincere gratitude for the contributions made by the Editorial Review Board, who were selected on the basis of their extensive experience and knowledge.

This book would not have been possible without the assistance and cooperation of my colleague, Géza T. Terézhalmy, DDS, MA. He is a wonderful coauthor, pleasant to work with, and encouraging in his demeanor. Special thanks to Heather Rybacki, our managing editor, and to Barrett Koger, our editor, who spearheaded the effort to get the second edition underway. In addition, much appreciation goes to Randy Huffines, DDS, at the Mountain Home Veteran's Hospital, Dental Clinic, for his suggestions on drugs used by dentists to add to the new edition.

Frieda A. Pickett, RDH, MS

This book is dedicated to my mentor, colleague, and friend, the late Dr. William K. Bottomley, who instilled in me an academic discipline essential for lifelong learning; to Frieda A. Pickett, RDH, MS, who conceived the idea of this book; and to my wife, Rebecca, without whose encouragement and support implementation of a project of this magnitude would not have been possible.

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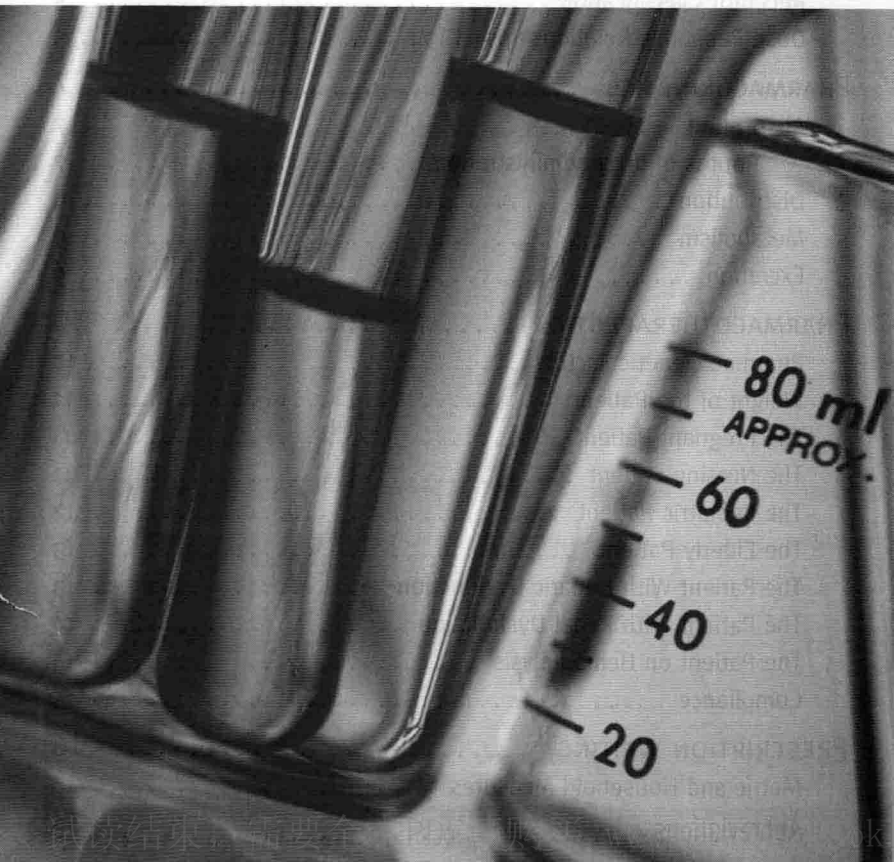

1 General Principles of Pharmacology

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INTRODUCTION

The science of pharmacology is the study of drugs. Historically, the clinician was responsible for information about the sources, physical and chemical properties, and compounding and dispensing of drugs. These activities are now delegated to pharmacologists and pharmacists. Today, the practitioner's responsibility requires the clinical application of this knowledge. Understanding how chemicals affect physiological homeostasis at the molecular level forms the basis for developing sound therapeutic strategies. Consequently, rational clinical use of therapeutic agents for prevention, diagnosis, and treatment of disease requires an understanding of basic pharmacological principles. These principles apply to all therapeutic agents (including vitamins, herbals, and nutritional supplements) and pertain to pharmacodynamic, pharmacokinetic, and pharmacotherapeutic variables.

PHARMACODYNAMICS

Pharmacodynamics is the study of molecular interactions between drugs and body constituents. It relates to the biochemical and physiological actions of drugs. Drugs circulating in the vascular compartment are carried to tissues. The first step in initiating a drug-induced effect is the formation of a complex between the drug and a cell component generally known as the ***drug receptor***. The ***receptor site*** where a drug acts to initiate a series of biochemical and physiological effects is the ***site of action*** of that drug. The molecular events that follow drug-receptor interactions are called the ***mechanisms of action*** of drugs. However, it should be understood that not all drugs produce their effects by interacting with specific receptors. A number of drugs form chemical bonds with small molecules, chelating agents, or metallic cations. A practical example of this type of drug-receptor interaction is the therapeutic neutralization of gastric acid by antacids. Many other drugs act by physiochemical mechanisms that are not yet understood.

DRUG-RECEPTOR INTERACTIONS

Drug receptors are cellular macromolecules (Figure 1-1). They may be metabolic or regulatory enzymes or coenzymes; proteins or glycoproteins associated with transport mechanisms; or structural and functional components of lipid membranes or nucleic acids. A single cell may have hundreds of receptor sites. Drugs attach to or interact with these receptor sites by ***covalent bonding***, ***ionic interactions***, ***hydrogen bonding***, or ***Van der Waals forces***, in descending order of bond strength, to produce a definable pharmacological response. Typically, drug-receptor binding is a combination of these interactions. Multiple weak forces, (e.g., multiple van der Waals interactions and a few hydrogen bonds) comprise most drug-receptor interactions. Ionic interactions and covalent bonding are much less common. The ***affinity*** of a drug for a particular receptor and the

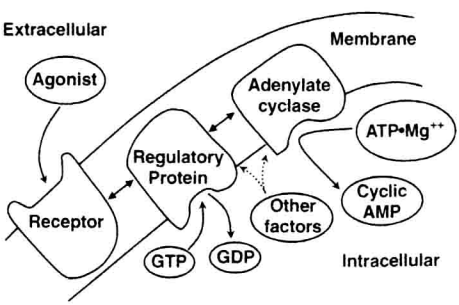

Figure 1-1. Drug receptors are cellular macromolecules.

type of binding is intimately related to the drug's chemical structure. Affinity is expressed by its dissociation constant (K_d), the concentration of a drug required in solution to achieve 50% occupancy of its receptors.

Most drug receptors have two conformational states that are in reversible equilibrium with one another: active state and inactive state. A drug that stabilizes the receptor in its active conformation is called an ***agonist***; a drug that prevents activation of the receptor by the agonist, and has no effect in the absence of the agonist, is referred to as an ***antagonist***. Some drugs cannot be neatly categorized as an agonist or an antagonist: such a drug may be classified as a ***partial agonist*** or an ***inverse agonist***. A partial agonist is a drug that binds to a receptor at its active site but produces only a partial response even when all the receptor sites are occupied. Some receptors are inherently stable in the active state, an inverse agonist acts by abrogating this intrinsic activity and stabilizes the receptor in the inactive state.

Antagonists can be divided into receptor and nonreceptor antagonists. A ***receptor antagonist*** binds either the agonist binding site or an allosteric site on a receptor. Binding the active site prevents the binding of the agonist to the receptor. Binding of the antagonist to an allosteric site either alters the affinity (K_d) of the agonist to the receptor or prevents the conformational change required to activate the receptor. Receptor antagonists can be classified as either competitive or noncompetitive. A ***competitive antagonist*** binds reversibly to the active site of a receptor; however, high concentrations of the agonist are able to overcome competitive antagonism. A ***noncompetitive antagonist*** binds to either the active site or an allosteric site of a receptor covalently, i.e., with very high affinity, and the binding is irreversible.

A ***nonreceptor antagonist*** does not bind to the receptor for the agonist, but it can still inhibit the agonist to initiate a response. A nonreceptor antagonist can be classified as a chemical antagonist or as a physiological antagonist. A ***chemical antagonist*** inactivates an agonist so that the agonist is no longer capable of binding to and activating the receptor. A ***physiological antagonist*** activates or blocks a receptor that mediates a response physiologically opposite to that of the receptor agonist.

Receptor Classification

Receptors are classified according to the type of drug that they interact with or according to the specific physiologic response produced by the drug-receptor complex. By evaluating the effects of different agonists in the presence of a given antagonist, receptors may also be subclassified. For example, cholinergic receptors can be activated either by muscarine or nicotine; however, only the response to muscarine is antagonized by atropine, while curare will only antagonize the response to nicotine. This evidence suggests that acetylcholine can bind to or activate at least two different receptor subtypes, which are either muscarinic or nicotinic. Similarly, receptors and receptor subtypes exist for many other agents. The number of any given receptor type or subtype on a cell may also vary. Certain disease states or drugs taken chronically and/or in large doses may increase (up-regulate) or decrease (down-regulate) the number of receptors and provide a degree of adaptability in the face of changing physiologic events.

Dose-Response Relationships

Pharmacodynamics is based on the concept of cellular drug-receptor binding. When a sufficient number of receptors are bound on a cell, the cumulative

effect of receptor occupancy becomes apparent in that cell. When the response occurs in many cells, the effect will be seen at the level of an organ. There are two major types of dose-response relationships: graded and quantal.

Graded dose-response relationships describe the effect of various doses of a drug on an individual. This relationship is expressed visually and mathematically with a graded dose-response curve. The curve is established by placing the logarithmic value for dosage (or ***log dose***) on the x-axis and the quantified response on the y-axis (Figure 1-2). Two important parameters can be deduced from the graded does-response curve: potency and efficacy. The ***potency (EC_{50})*** of a drug is the concentration at which the drug elicits 50% of its maximal response and is related to the affinity of that drug to its receptor. The ***efficacy (E_{max})*** is the maximal response produced by the drug and is related to the intrinsic activity of that drug once a drug-receptor complex is formed. The dose of a drug associated with (E_{max}) is called the ***ceiling dose*** of that drug.

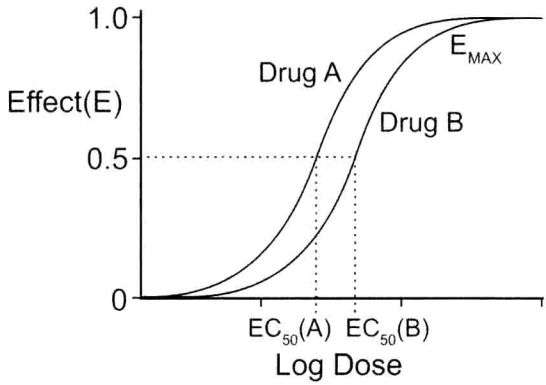

Figure 1-2. Graded dose-response curves. The upper plateau of the curve represents the E_{max} of a drug. EC_{50} is the potency of a drug. In the figure, drug A is more potent than drug B, yet drug A and drug B exhibit the same efficacy. Clearly, EC_{50} and E_{max} are not intrinsically related.

Quantal dose-response relationships show the average effect of a drug, as a function of its concentration, in a population of individuals. This relationship is expressed visually and mathematically with a quantal dose-response curve. The curve is established by placing

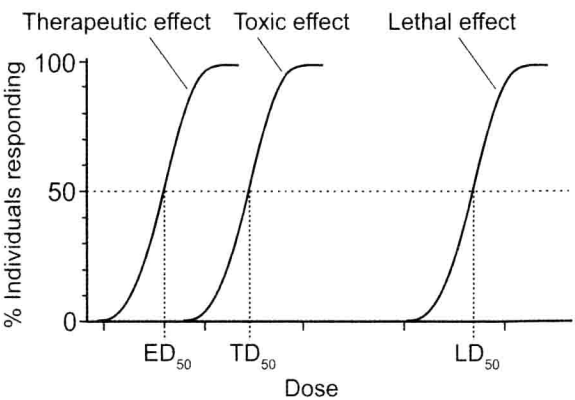

Figure 1-3. Quantal dose-response curves demonstrate the average effect of a drug, as a function of its concentration, in a population of individuals. ED_{50}, TD_{50}, and LD_{50} represent the dose required to produce a beneficial, toxic, and lethal effect in 50% of the individuals within the same population, respectively.

the logarithmic value for dosage (log dose) on the x-axis and the response defined as either present or not present (quantal, not graded) in the percentage of individuals responding on the y-axis (Figure 1-3). Three important parameters can be deduced from the quantal dose-response curve: effectiveness (therapeutic effect), toxicity (adverse effect), and lethality (lethal effect). The doses that produce these responses in 50% of a population are known as the ***median effective dose (ED_{50})***, ***median toxic dose (TD_{50})***, and ***medial lethal dose (LD_{50})***, respectively. The ***therapeutic window*** is the range of doses of a drug that elicits a therapeutic response, without unacceptable adverse drug effects (toxicity) in a patient population. The therapeutic window can be quantified by the ***therapeutic index (TI)***, expressed mathematically as $TI = TD_{50}/ED_{50}$. A large TI reflects a large therapeutic window and a small TI reflects a narrow therapeutic window.

PHARMACOKINETICS

To produce an effect, most drugs must pass through biological membranes to gain access to their receptor(s). Small, water-soluble substances may pass through aqueous channels by a process known as ***filtration***. Most drugs, however, are weak acids or weak bases too large to pass through aqueous channels. The passage of these drug molecules across cell membranes is achieved primarily by ***passive diffusion*** along a concentration gradient. Other drugs may cross biological membranes by ***facilitated diffusion*** or ***active transport***. In these processes a drug is carried across biological membranes by forming a complex with a component of the cell membrane, the complex is carried through the membrane, the drug is released, and the carrier returns to the original surface to repeat the process. ***Facilitated diffusion*** does not require energy and does not proceed against a concentration gradient. Conversely, ***active transport*** is characterized by selectivity, competitive inhibition, requirement for energy, saturability, and movement against an electrochemical gradient. Some water-insoluble substances are engulfed by the cell membrane and are released unchanged in the cytoplasm by the process known as ***pinocytosis***.

ABSORPTION

Most drugs are weak acids or weak bases that diffuse through the lipid component of the cell membrane as a function of the drug's molecular weight, lipid solubility coefficient, pK_a (the pH at which a drug is 50% ionized and 50% un-ionized), and concentration. In general, drugs with a small molecular weight will cross biological membranes more readily than drugs with a large molecular weight. The nonpolar, un-ionized form of a drug will diffuse across biological membranes more readily than its ionized, polar fraction. Drugs administered in high concentration are more readily absorbed than low concentrations of the same drug. A drug's formulation and its route of administration further influence absorption.

Routes of drug administration

Enteral. The oral route is the most common, convenient, and economical method of drug administration. It is also the most unpredictable. When a drug is administered enterally, its rate of absorption into the systemic circulation is influenced by the inherent characteristics of the drug, the pH of the gastrointestinal tract, the presence of food in the stomach, gastric motility, splanchnic blood flow, and, importantly, patient compliance with the prescribed drug regi-