Introduction to Pharmaceutical Dosage Forms

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Dosage Forms and Routes of Administration

DRUG substances are seldom administered in their natural or pure state, but rather as part of a formulation in combination with one or more nonmedicinal agents that serve varied and specialized pharmaceutical functions. Through selective use of these nonmedicinal agents, referred to as *pharmaceutic ingredients*, aids, adjuncts, or necessities, pharmaceutical preparations of various types result. The pharmaceutic ingredients solubilize, suspend, thicken, dilute, emulsify, stabilize, preserve, color, flavor, and fashion the many and varied medicinal agents into efficacious and appealing pharmaceutical preparations. Each different type of preparation is unique in its physical and pharmaceutical characteristics and in the final form in which the drug is presented to the patient. These varied preparations, which provide the manufacturing pharmacist with the challenges of formulation and the physician with the choice of pharmaceutical types, are termed "dosage forms." The general area of study which concerns itself with the physical, chemical, and biological factors which influence the formulation, manufacture, stability, and effectiveness of pharmaceutical dosage forms is termed *pharmaceutics*.

The Need for Dosage Forms

The potent nature and low dosage of most of the drugs in use today precludes any expectation that the general public could safely obtain the appropriate dose of a drug from the bulk material. The vast majority of drug substances are administered in milligram amounts, much too small to be weighed on anything but a sensitive laboratory balance. For instance, how could the layman accurately obtain the 325 mg of aspirin found in the common aspirin tablet from a bulk supply of aspirin? He couldn't. Yet, compared with many other drugs, the dose of aspirin is formidable (Table 3-1). For example, the dose of ethinyl estradiol, 0.05 mg, is 1/6500 the amount of aspirin in an aspirin tablet. To put it another way, 6500 ethinyl estradiol tablets, each containing 0.05 mg of drug, could be made from an amount of ethinyl estradiol equal to the amount of aspirin in just one aspirin tablet. When the dose of the drug is minute, as that for ethinyl estradiol, solid dosage forms such as tablets and capsules must be prepared with fillers or diluents so that the size of the resultant dosage unit is large enough to pick up with the fingertips.

In addition to providing the mechanism for the safe and convenient delivery of accurate dosage, dosage forms are needed for the following and other reasons:

1. For the protection of a drug substance from the destructive influences of atmospheric oxygen or moisture (e.g. coated tablets, sealed ampules).
2. For the protection of a drug substance from the destructive influence of gastric acid

Table 3-1. Examples of Some Drugs with Relatively Low Usual Doses

Drug	*Usual Dose mg*	*Category*
Lithium Carbonate	300	Antidepressant
Ferrous Sulfate	300	Hematinic
Erythromycin	250	Antibacterial
Ampicillin	250	Antibacterial
Tetracycline HCl	250	Antibacterial
Nitrofurantoin	100	Antibacterial (urinary)
Digitalis	100	Cardiotonic
Pentobarbital Sodium	100	Hypnotic
Propoxyphene HCl	65	Analgesic
Hydrochlorothiazide	50	Diuretic
Codeine Phosphate	30	Analgesic
Phenobarbital	30	Sedative
Chlorpromazine HCl	25	Tranquilizer
Diphenhydramine HCl	25	Antihistaminic
Morphine Sulfate	10	Narcotic analgesic
Prednisolone	5	Adrenocortical steroid
Chlorpheniramine maleate	4	Antihistaminic
Colchicine	0.5	Gout Supressant
Diethylstilbestrol	0.5	Estrogen
Atropine Sulfate	0.4	Anticholinergic
Nitroglycerin	0.4	Antianginal
Ergonovine Maleate	0.2	Oxytocic
Digitoxin	0.1	Cardiotonic (maintenance)
Ethinyl Estradiol	0.05	Estrogen

after oral administration (e.g. enteric coated tablets).

3. To conceal the bitter, salty, or obnoxious taste or odor of a drug substance (e.g. capsules, coated tablets, flavored syrups).
4. To provide liquid preparations of substances that are either insoluble or unstable in the desired vehicle (e.g. suspensions).
5. To provide liquid dosage forms of substances soluble in the desired vehicle (e.g. solutions).
6. To provide extended drug action through controlled release mechanisms (e.g. various controlled release tablets, capsules and suspensions).
7. To provide optimal drug action from topical administration sites (e.g. ointments, creams, ophthalmic, ear, and nasal preparations).
8. To provide for the insertion of a drug into one of the body's orifices (e.g. rectal or vaginal suppositories).
9. To provide for the placement of drugs within body tissues (e.g. injections).
10. To provide for optimal drug action through inhalation therapy (e.g. inhalants and inhalation aerosols).

In addition to the above, many dosage forms permit ease of drug identification through distinctiveness of color, shape, or identifying markings.

The Variety of Dosage Forms

There are many different forms into which a medicinal agent may be placed for the convenient and efficacious treatment of disease. Drugs can be prepared for administration by every conceivable route, and the appropriate pharmaceutical preparation formulated to insure maximum therapeutic response. Tables 3-2 and 3-3 present the various routes of drug administration and the most commonly utilized dosage forms.

Some individual medicinal agents are effective therapeutic agents for maladies of various parts of the body and are formulated into a half dozen or more dosage forms of varying strengths, each having the particular pharmaceutical characteristics which lend themselves best to a specific application. One such versatile drug is prednisolone, a synthetic adrenocortical steroid, used primarily for its anti-inflammatory activity. In the USP XX, prednisolone and its various chemical forms are officially recognized as:

(a) Prednisolone, the chemical powder used in pharmaceutical compounding, particularly in the preparation of (b) and (c).
(b) Prednisolone Tablets, used orally for the systemic action of prednisolone.
(c) Prednisolone Cream, for topical application to the skin.
(d) Prednisolone Tebutate, a slightly soluble in water compound, used in the form of a sterile suspension as an intra-articular, intrabursal, and soft-tissue injection.
(e) Prednisolone Acetate, the acetate ester form of prednisolone, used primarily in the preparation of (f).
(f) Sterile Prednisolone Acetate Suspension,

Table 3-2. Routes of Drug Administration

Term	*Site*
oral	mouth
peroral (per os[1])	gastrointestinal tract via mouth
sublingual	under the tongue
parenteral	other than the gastrointestinal tract (by injection)
intravenous	vein
intraarterial	artery
intracardiac	heart
intraspinal or intrathecal	spine
intraosseous	bone
intraarticular	joint
intrasynovial	joint-fluid area
intracutaneous or intradermal	skin
subcutaneous	beneath the skin
intramuscular	muscle
epicutaneous (topical)	skin surface
conjunctival	conjunctiva
intraocular	eye
intranasal	nose
aural	ear
intrarespiratory	lung
rectal	rectum
vaginal	vagina
urethral	urethra

[1]The abbreviation "p.o." is commonly employed on prescriptions to indicate to be swallowed.

Table 3-3. Dosage Form Application

Route of Administration	*Primary Dosage Forms*
oral	tablets capsules solutions syrups elixirs suspensions magmas gels powders
sublingual	tablets troches or lozenges
parenteral	solutions suspensions
epicutaneous	ointments creams pastes plasters powders aerosols lotions solutions
conjunctival	ointments
intraocular/ intraaural	solutions suspensions
intranasal	solutions sprays inhalants ointments
intrarespiratory	aerosols
rectal	solutions ointments suppositories
vaginal	solutions ointments emulsion foams tablets suppositories
urethral	solutions suppositories

employed as an intra-articular and intramuscular injection.

(g) Prednisolone Sodium Phosphate, a water soluble salt form of prednisolone, used primarily in the preparation of (h) and (i).

(h) Prednisolone Sodium Phosphate Injection, an aqueous solution used for intravenous or intramuscular injection.

(i) Prednisolone Sodium Phosphate Ophthalmic Solution, an aqueous solution for topical application to the eye.

(j) Prednisolone Succinate, a slightly soluble in water compound, used in the preparation of (k).

(k) Prednisolone Sodium Succinate for Injection, a sterile powder, prepared from sodium succinate with the aid of sodium carbonate. At the time of use it is prepared into a solution and used by intramuscular or intravenous injection.

By creating special chemical forms of the basic chemical prednisolone, research pharmacists have facilitated the preparation of effective anti-inflammatory pharmaceuticals of prednisolone for use orally, by injection as a

suspension or solution, and for topical application to the skin and eye.

In addition to prednisolone, other drugs are prepared in numerous dosage forms and strengths for the efficacious and convenient treatment of disease (see Figure 3-1). Before a medicinal agent is formulated into one or more dosage forms, among the factors which must be considered are such therapeutic matters as: the nature of the illness, the manner in which it is generally treated, locally or through systemic action, and the age and anticipated condition of the patient.

Therapeutic Considerations in Dosage Form Design

The nature of the disease or illness against which the drug is intended is an essential consideration in deciding which dosage forms of a drug to prepare and market. Such basic questions as whether the disease is best treated systemically or locally must be answered, and the most appropriate dosage forms prepared and evaluated in clinical trials. Assessments must be made as to whether the illness is best treated with prompt-, slow-, short-, or long-acting pharmaceuticals. If there is the remotest chance that a given drug may have application to an emergency situation or one in which the patient is comatose, or unlikely to take oral medication, a form suitable for parenteral administration may be developed. If the illness is one that can generally be treated safely through the self-administration of the drug, manufacturer's oblige by placing the drug in compact dosage units such as tablets or capsules or in easily administered liquid forms. In the vast majority of instances, drug manufacturers prepare a single medicinal agent into several dosage forms, partly to satisfy the personal preference of the physician or patient and partly to meet the peculiar needs or requirements of a certain situation. For instance, drugs used to combat nausea and vomiting may be taken prophylactically in tablet form, as before boarding an airplane or for the morning sickness of pregnancy, but this form may be of little value if given during the course of the illness because it may be spewed with the vomitus. For this reason suppositories are also made available for use when required. They are particularly useful in treating infants. Each drug has its own individual characteristics relating to drug absorption. Some may be well absorbed from a given route of administration, whereas others may be poorly absorbed. Each drug must be individually evaluated and the most efficacious routes determined and dosage forms prepared.

Drugs intended to provide localized effects are applied directly to the site of their intended action. This includes most of the products utilized in the eye, ear, nose, throat, as well as those applied to the skin or placed in the vagina or rectum or swallowed for localized effects within the gastrointestinal tract.

The Age of the Patient

The age of the intended patient has a pronounced influence on the types of dosage forms prepared for a given drug. For infants and children under 5 years of age, pharmaceutical liquids rather than solid dosage forms are preferred for oral administration. These liquids, which are generally flavored aqueous solutions, syrups or suspensions, are usually administered directly into the infant's or child's mouth or incorporated with his food (Fig. 3-2). A single liquid pediatric preparation may be used for infants and children of all ages, with the dose of the drug varied by the volume administered. When an infant is in the throes of a vomiting crisis, is gagging, has a productive cough, or is simply rebellious, there may be some question as how much of the medicine administered is actually swallowed and how much is expectorated. In such instances, injections may be required. Infant size rectal suppositories may also be employed although drug absorption from the rectum is erratic and undependable.

The oral route is preferred when administering medication to children. However, with many children there is a problem of compliance with the prescribed dosage regimen. In these instances, dosage forms which allow reduced frequency of administration may be employed to advantage over those requiring greater frequency of administration. This may be particularly true for children who may be scheduled to take medication while at school. In instances in which compliance is an absolute necessity and cannot be guaranteed through self-administered oral medication, parenteral therapy may be required.

During early childhood and sometimes in later years, a youngster may have difficulty

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