CHAPTER 4

PHARMACEUTICS AND DRUG DELIVERY

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Abstract

Pharmaceutics converts an active pharmaceutical ingredient into effective dosage forms through scientific principles of drug delivery. Dosage form design balances pharmacological requirements with patient factors, creating solid forms (tablets, capsules), liquid preparations, semisolids, and specialized delivery systems, each requiring specific formulation approaches addressing stability, release kinetics, and manufacturing scalability. Drug absorption mechanisms determine therapeutic effectiveness through complex processes influenced by physicochemical properties, physiological variables, and formulation factors, with bioavailability measures quantifying the fraction of administered drug reaching systemic circulation. Novel drug delivery systems extend beyond conventional formulations to provide targeted delivery, controlled release, and enhanced stability through liposomal encapsulation, nanoparticle carriers, transdermal patches, implantable systems, and 3D-printed medications tailored to individual patient needs. Pharmaceutical excipients serve essential functions beyond merely completing formulations, acting as diluents, binders, disintegrants, lubricants, coating materials, preservatives, and solubilizers, with careful selection required to ensure compatibility, stability, and proper drug release while avoiding potential allergic reactions or interactions.

Keywords: *Formulation; Drug Release; Delivery Systems; Physicochemical Properties; Product Development*

Learning Objectives

After completion of the chapter, the learners should be able to:

- Classify dosage forms based on physical state, route of administration, and release characteristics.
- Analyze factors affecting drug dissolution, absorption, and bioavailability across different physiological barriers.
- Compare controlled-release technologies including matrix systems, reservoir devices, and osmotic pump mechanisms.
- Select appropriate excipients for specific formulations based on their functional properties and compatibility with active ingredients.
- Evaluate novel drug delivery approaches including nanoparticles, liposomes, and targeted delivery systems for specific therapeutic applications.
- Design appropriate beyond-use dating for compounded preparations based on stability considerations and USP guidelines.

DOSAGE FORM DESIGN

Dosage form design involves the systematic development of drug delivery systems that optimize therapeutic outcomes while addressing patient needs, manufacturing considerations, and commercial viability. This multidisciplinary process integrates pharmaceutical science with engineering principles to create formulations that deliver medications effectively, safely, and conveniently.

The rational design of dosage forms begins with preformulation studies that characterize the physicochemical properties of the active pharmaceutical ingredient (API). These properties—including solubility, partition coefficient, pKa, crystal structure, particle size, and stability profile—establish constraints and opportunities that guide formulation decisions. For instance, a drug with poor aqueous solubility might benefit from particle size reduction, amorphization, or incorporation into lipid-based delivery systems, while a moisture-sensitive compound might require protective coating or packaging strategies.

Patient-centered considerations significantly influence dosage form selection and design. The target patient population's characteristics—including age, comorbidities, dexterity limitations, and medication adherence challenges—inform decisions regarding route of administration, dosage form size, taste characteristics, and ease of use. Pediatric formulations, for example, often prioritize taste masking, flexible dosing options, and age-appropriate administration routes, while geriatric formulations might emphasize ease of swallowing, simplified dosing regimens, and packaging that accommodates limited dexterity.

Table 4.1: Common Dosage Forms and Their Characteristics

Dosage Form	Onset of Action	Advantages	Disadvantages
Tablets	30-60 minutes	Convenience, stability, accurate dosing	First-pass effect, GI irritation
Capsules	30-60 minutes	Taste masking, easy to swallow	Manufacturing complexity
Solutions	15-30 minutes	Rapid absorption, easy administration	Stability issues, taste concerns
Suspensions	15-30 minutes	Taste masking, insoluble drugs	Sedimentation, shaking required
Immediate-release	30-60 minutes	Rapid effect, simple formulation	Short duration, frequent dosing
Extended-release	1-2 hours	Reduced dosing frequency, steady levels	Complex formulation, higher cost
Delayed-release	Variable	Targeted release, protect from acid	Manufacturing complexity
Injections	Seconds to minutes	Rapid effect, high bioavailability	Pain, sterility requirements
Inhalers	5-15 minutes	Direct to target, reduced systemic effects	Technique-dependent, local irritation

Dosage Form	Onset of Action	Advantages	Disadvantages
Transdermal	Hours	Extended delivery, avoids first-pass	Skin irritation, limited applicability
Suppositories	15-30 minutes	Avoids first-pass, useful when NPO	Patient acceptance, melting concerns
Creams	Variable	Easy application, moisturizing	Greasy feel, limited penetration
Ointments	Variable	Occlusive, enhanced penetration	Greasy, staining potential
Gels	Variable	Less greasy, transparent	Drying effect, stinging potential
Patches	Hours	Controlled release, convenience	Adhesion issues, skin irritation
Lozenges	15-30 minutes	Local effect, slow dissolution	Limited to certain drugs
Implants	Days to months	Extended release, adherence	Surgical procedure, removal concerns

Solid Oral Dosage Forms

Tablets remain the most widely used pharmaceutical dosage form due to their manufacturing efficiency, dosing precision, stability advantages, and patient acceptance. Tablet design involves selection and optimization of multiple components: active ingredients, diluents, binders, disintegrants, lubricants, glidants, and potentially coating materials. Each component serves specific functions that collectively determine the tablet's physical integrity, disintegration profile, dissolution characteristics, and ultimately its *in vivo* performance.

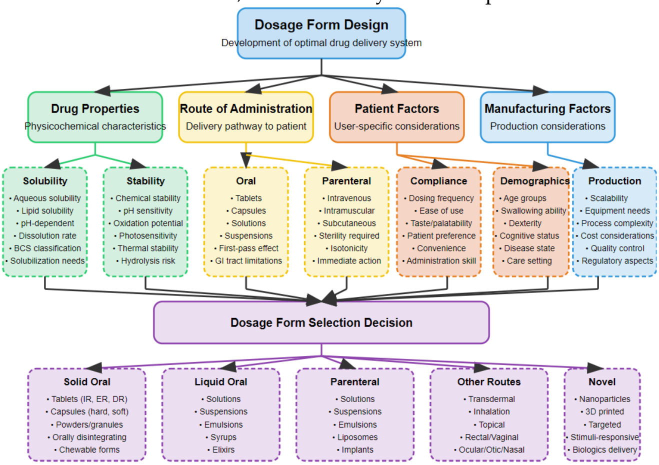

Figure 4.1: Dosage Form Design Decision

Direct compression represents the simplest and most economical tablet manufacturing method, suitable for stable, freely flowing materials with good compressibility. This approach involves simple blending of ingredients followed by compression, avoiding the complexity and potential stability challenges associated with wet processes. However, many APIs lack the flow and compression properties necessary for direct compression, necessitating alternative approaches.

Wet granulation improves the flow and compression characteristics of powder blends by creating larger agglomerates with more uniform composition. This process involves mixing the API with excipients, adding a granulating liquid to form a moist mass, wet-milling or screening to achieve uniform granule size, drying to remove the granulating liquid, and finally dry-milling to optimize granule size distribution. While more complex than direct compression, wet granulation accommodates a wider range of drug properties and often produces tablets with superior content uniformity.

Dry granulation provides an intermediate option for moisture-sensitive materials, using mechanical pressure rather than liquid to create granules. Roller compaction, the most common dry granulation method, compresses powder blends between counter-rotating rollers to form dense sheets (ribbons) that are subsequently milled into granules. This approach improves flow properties and content uniformity without exposure to moisture or heat, though typically producing granules with lower binding capacity than wet granulation methods.

Capsules provide an alternative solid oral dosage form, particularly valuable for drugs with poor compression properties or requirements for rapid dissolution. Hard gelatin capsules accommodate powder blends or granules, while soft gelatin capsules typically contain liquid or semi-solid formulations that enhance solubility and dissolution of poorly water-soluble compounds. Both capsule types offer advantages including taste masking, reduced irritant contact with oral mucosa, and distinctive appearance that aids product identification.

Liquid Dosage Forms

Solutions represent the simplest liquid dosage forms, with the drug completely dissolved in a suitable solvent system. These formulations offer rapid drug availability and dosing flexibility but often present stability challenges and may require inclusion of preservatives, antioxidants, buffers, or other functional excipients. The selection of solvent systems balances considerations of drug solubility, stability, palatability, and toxicity, often necessitating co-solvent mixtures to achieve optimal performance.

Suspensions contain finely divided solid drug particles dispersed in a liquid vehicle, providing options for drugs with limited solubility or stability in solution. The physical stability of suspensions depends on particle size control, viscosity adjustment, and incorporation of surfactants or polymers that modify particle-particle interactions. Structured vehicles containing thixotropic agents help prevent sedimentation during storage while allowing flow during administration, improving dose uniformity and patient acceptability.

Emulsions consist of two immiscible liquids, with one dispersed as droplets within the other, stabilized by emulsifying agents. Oil-in-water (o/w) emulsions typically offer better palatability and can be diluted with aqueous fluids, while water-in-oil (w/o) emulsions provide prolonged contact with absorption surfaces and protection for water-sensitive compounds. Microemulsions and self-emulsifying drug delivery systems (SEDDS) represent advanced approaches that enhance bioavailability of poorly water-soluble drugs through formation of small droplets with high surface area and solubilization capacity.

Parenteral solutions and suspensions require exceptional quality standards due to their administration routes that bypass natural protective barriers. These formulations must meet requirements for sterility, endotoxin limits, particulate matter control, and compatibility with body tissues and fluids. Tonicity adjustment prevents tissue damage from osmotic effects, while pH adjustment optimizes stability and minimizes injection pain. Selection of appropriate preservatives for