

# Introduction to Pharmaceutical Dosage Forms

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FOURTH EDITION

*200th  
Anniversary*  
1785 - 1985



LEA & FEBIGER · *Philadelphia*

1985

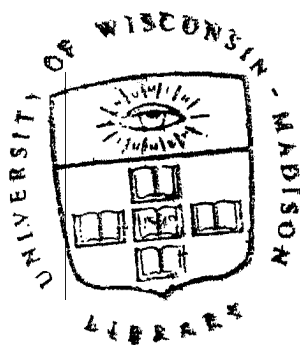
Lea & Febiger  
600 Washington Square  
Philadelphia, PA 19106-4198  
U.S.A.  
(215) 922-1330

**Library of Congress Cataloging in Publication Data**

Ansel, Howard C., 1933—  
Introduction to pharmaceutical dosage forms.

Includes bibliographies and index.

1. Drugs—Dosage forms. I. Title. [DNLM: 1. Dosage  
Forms. 2. Drugs—administration & dosage. QV 785 A618i]  
RS200.A57 1985 615'.1 84-9732  
ISBN 0-8121-0956-2



*1st Edition, 1969*  
*Reprinted, 1972*  
*2nd Edition, 1976*  
*Reprinted, 1978*  
*3rd Edition, 1981*  
*Reprinted, 1982*  
*4th Edition, 1985*

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PRINTED IN THE UNITED STATES OF AMERICA  
Print No. 4 3 2 1

Noven Ex. 1016  
Page 2 of 36

# Dosage Form Design: Pharmaceutical Ingredients, Product Formulation, and Current Good Manufacturing Practice

THE PROPER design of a dosage form requires consideration of the physical, chemical and biological characteristics of all of the drug substances and pharmaceutical ingredients to be used in fabricating the product. The drug and pharmaceutical materials utilized must be compatible with one another to produce a drug product that is stable, efficacious, attractive, easy to administer and safe. The product should be manufactured under appropriate measures of quality control and packaged in containers that contribute to product stability. The product should be labeled to promote correct use and be stored under conditions that contribute to maximum shelf life.

Methods for the preparation of specific types of dosage forms are described in subsequent chapters. This chapter presents some general considerations regarding pharmaceutical ingredients, drug product formulation, stability, preservation, flavoring, coloring, packaging, storage, and standards for good manufacturing practice.

## Pharmaceutical Ingredients

In order to prepare a drug substance into a final dosage form, pharmaceutical ingredients are required. For example, in the preparation of pharmaceutical solutions, one or more *solvents* are utilized to dissolve the drug substance, *preservatives* may be added to prevent microbial growth, *stabilizers* may be used to prevent drug

decomposition, and *colorants* and *flavorants* added to enhance product appeal. In the preparation of tablets, *diluents* or *fillers* are commonly added to increase the bulk of the formulation, *binders* to cause the adhesion of the powdered drug and pharmaceutical substances, *antiadherents* or *lubricants* to assist the smooth tableting process, *disintegrating agents* to promote tablet break-up after administration, and coatings to improve stability, control disintegration, or to enhance appearance. Ointments, creams, and suppositories achieve their characteristic features due to the pharmaceutical *bases* which are utilized. Thus, for each dosage form, the pharmaceutical ingredients establish the primary features of the product, and contribute to the physical form, texture, stability, taste and overall appearance.

Table 5-1 presents the principal categories of pharmaceutical ingredients, with examples of some of the official agents currently used.

## General Considerations in Drug Product Formulation

In dealing with the problem of formulating a drug substance into a proper dosage form, research pharmacists employ knowledge that has been gained through experience with other similar drugs and through the proper utilization of the disciplines of the physical, chemical, and biological sciences. The early stages of any new

Table 5-1. Examples of Official Pharmaceutical Ingredients

<i>Ingredient Type</i>	<i>Definition</i>	<i>Examples</i>
<i>Acidifying Agent</i>	Used in liquid preparations to provide acidic medium for product stability.	acetic acid hydrochloric acid nitric acid
<i>Alkalinizing Agent</i>	Used in liquid preparations to provide alkaline medium for product stability.	ammonia solution ammonium carbonate potassium hydroxide sodium borate sodium carbonate sodium hydroxide trolamine
<i>Adsorbent</i>	An agent capable of holding other molecules onto its surface by physical or chemical (chemisorption) means.	powdered cellulose activated charcoal
<i>Aerosol Propellant</i>	An agent responsible for developing the pressure within an aerosol container and expelling the product when the valve is opened.	dichlorodifluoromethane dichlorotetrafluoroethane trichloromonofluoromethane
<i>Air Displacement</i>	An agent which is employed to displace air in a hermetically sealed container to enhance product stability.	nitrogen
<i>Antifungal Preservative</i>	Used in liquid and semi-solid preparations to prevent the growth of fungi.	benzoic acid butylparaben ethylparaben methylparaben propylparaben sodium benzoate sodium propionate
<i>Antimicrobial Preservative</i>	Used in liquid and semi-solid preparations to prevent the growth of microorganisms.	benzalkonium chloride benzethonium chloride benzyl alcohol cetylpyridinium chloride chlorobutanol phenol phenylethyl alcohol phenylmercuric nitrate thimerosal
<i>Antioxidant</i>	An agent which inhibits oxidation and thus is used to prevent the deterioration of preparations by the oxidative process.	ascorbyl palmitate butylated hydroxyanisole butylated hydroxytoluene hypophosphorous acid monothioglycerol propyl gallate sodium bisulfite sodium formaldehyde sulfoxylate sodium metabisulfite
<i>Buffering Agent</i>	Used to resist change in pH upon dilution or addition of acid or alkali.	potassium metaphosphate potassium phosphate, monobasic sodium acetate

Table 5-1. Continued

Ingredient Type	Definition	Examples
Chelating Agent	A substance that forms stable complexes with metals. Chelating agents are used in some liquid pharmaceuticals as stabilizers to complex heavy metals which might promote instability. In such use they are also called <i>sequestering</i> agents.	edetate disodium edetic acid
Colorant	Used to impart color to pharmaceutical preparations.	erythrosine (FD&C Red No. 3) caramel ferric oxide, red
Emulsifying Agent	Used to promote and maintain the dispersion of finely subdivided particles of a liquid in a vehicle in which it is immiscible.	acacia sorbitan monooleate polyoxyethylene 50 stearate
Encapsulating Agent	Used to form thin shells for the purpose of enclosing a drug substance or drug formulation for ease of administration.	gelatin cellulose acetate phthalate
Flavorant	Used to impart a pleasant flavor and often odor to a pharmaceutical preparation.	anise oil cinnamon oil cocoa menthol orange oil peppermint oil vanillin
Humectant	Used to prevent the drying out of preparations—particularly ointments and creams—due to the agent's ability to retain moisture.	glycerin propylene glycol sorbitol
Levigating Agent	A liquid used as an intervening agent to reduce the particle size of a drug powder by grinding together, usually in a mortar.	mineral oil
Ointment Base	The semisolid vehicle into which drug substances may be incorporated in preparing medicated ointments.	lanolin hydrophilic ointment polyethylene glycol ointment petrolatum hydrophilic petrolatum white ointment yellow ointment rose water ointment
Solvent	An agent used to dissolve another pharmaceutical substance or a drug in the preparation of a solution.	alcohol isopropyl alcohol mineral oil oleic acid peanut oil purified water water for injection sterile water for injection sterile water for irrigation
Stiffening Agent	Used to increase the thickness or hardness of a pharmaceutical preparation, usually an ointment.	cetyl alcohol paraffin white wax yellow wax

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