

Pharmaceutics

The science of dosage form design

Edited by M E Aulton

Churchill Livingstone 

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Medical Division of Longman Group UK Limited
Distributed in the United States of America by
Churchill Livingstone Inc., 650 Avenue of the Americas,
New York, 10011, and associated companies, branches
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(Churchill Livingstone, Robert Stevenson House, 1-3
Baxter's Place, Leith Walk, Edinburgh EH1 3AF), or a
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Kingdom issued by the Copyright Licensing Agency Ltd,
90 Tottenham Court Road, London, W1P 9HE.

First published 1988

Reprinted 1989

Reprinted 1990

Reprinted 1991

Reprinted 1992

ISBN 0-443-03643-8

British Library Cataloguing in Publication Data

Pharmaceutics: the science of dosage form
design.

1. Pharmaceutics

I. Aulton, Michael E.

615'.19 RS403

Library of Congress Cataloging in Publication Data

Pharmaceutics: the science of dosage form design.

Replaces: Cooper and Gunn's tutorial pharmacy.

6th ed. 1972.

Includes bibliographies and index.

1. Drugs — Design of delivery systems. 2. Drugs
— Dosage forms. 3. Biopharmaceutics.

4. Pharmaceutical technology. 5. Chemistry,
Pharmaceutical. 6. Microbiology, Pharmaceutical.

I. Aulton, Michael E.

[DNLM: 1. Biopharmaceutics. 2. Chemistry,
Pharmaceutical. 3. Dosage Forms. 4. Technology,
Pharmaceutical. 5. Microbiology, Pharmaceutical.

QV 785 P5366]

RS420.P48 1987 615.5'8 86-25888

Printed in Hong Kong
CPP/05

The
publisher's
policy is to use
paper manufactured
from sustainable forests

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Parenteral products

THE BIOPHARMACY OF INJECTIONS

Routes of administration

Intracutaneous or intradermal route

Subcutaneous or hypodermic route

Intramuscular route

Intravascular routes

Intracardiac route

Intraspinal routes

Intra-articular and intrabursal routes

Ophthalmic routes

Bioavailability of drugs from injections

FORMULATION OF INJECTIONS

Volume of the injection

The vehicle

Water and pyrogens

Water-miscible vehicles

Water-immiscible vehicles

Osmotic pressure

Intravascular injections

Intrathecal injections

Intramuscular injections

Intracutaneous injections

Subcutaneous injections

Hydrogen ion concentration (pH)

To increase the stability of the injection

To minimize pain, irritation and necrosis on injection

To provide unsatisfactory conditions for growth of micro-organisms

To enhance physiological activity

Buffers

Specific gravity of injections

Suspensions for injection

Wettability

Sedimentation rate

Claying

Size and shape of particles

Thixotropy

Preparation of aqueous suspension injections

Suspensions in oily vehicles

Addition of a gelling agent

Particle size

Emulsions for injection

Intravenous therapy and emulsions

Colloidal dispersions and solubilized products

QUALITY ASSURANCE OF INJECTIONS

Microbiological preservation

The use of bactericides in single-dose injections

The use of bactericides in multiple-dose injections

Bactericides suitable for aqueous injections

Bactericides suitable for oily injections

Limitations in the use of bactericides

Incompatibilities of common bactericides

Chemical stability of the medicament

Adjustment of pH

Addition of a reducing agent or antioxidant

Replacement of air by an inert gas

Use of a sequestering agents

Inclusion of specific stabilizers

Calcium Gluconate Injection BP

Sodium Bicarbonate Injection BP

Mersalyl Injection BP

Limitations in the use of additives

Particulate contamination

PACKAGING OF INJECTIONS

Containers for injections

Ideal properties

Types of container

Single-dose versus multiple-dose containers

Materials for injection containers

Glass

Types of glass

Associated problems for parenterals*Plastics***Types of plastics****Associated problems for parenterals***Closures***Types and properties of closure materials****Associated problems for parenterals**

STERILIZATION OF INJECTIONS

Injections are sterile products intended for administration into the bodily tissues. Their formulation involves careful consideration of all the following inter-relating factors:

- 1 the proposed route of administration,
- 2 the volume of the injection,
- 3 the vehicle in which the medicament is to be dissolved or suspended,
- 4 the osmotic pressure of the solution,
- 5 the use of preservative,
- 6 the pH of the solution,
- 7 the stability of the medicament and methods of sterilization,
- 8 the specific gravity of the injection,
- 9 the properties of suspensions for injection,
- 10 the properties of emulsions for injection,
- 11 containers or closures for injections,
- 12 particulate contamination,
- 13 biopharmacy of injections.

THE BIOPHARMACY OF INJECTIONS

Injections are administered into the body by many routes. The route of administration affects the formulation and biopharmaceutics of the preparation. There now follows a description of routes of administration to clarify nomenclature used throughout the rest of the chapter. Fig. 21.1 shows the sites of injection.

Routes of administration

The most important routes are as follows.

Intracutaneous or intradermal route

Injections are made into the skin between the

inner layer (dermis) and the outer layer (epidermis). The volume that can be injected intradermally is small, usually 0.1–0.2 ml, due to the poor vascularity of the site which gives poor dispersion of the drug, and leaves blisters or weals at the site of the injection. The route is used mainly for diagnostic tests.

Subcutaneous or hypodermic route

Injections are made under the skin into the subcutaneous tissue. The volume injected is usually 1 ml or less. This route is not used for aqueous suspensions or oily suspensions and fluids since these would cause pain and irritation at the injection site.

Intramuscular route

Injections are made by passing the needle into the muscle tissue via the skin, subcutaneous tissue and membrane enclosing the muscle. The volume is usually no greater than 2 ml and should not exceed 4 ml. This route is used for aqueous and oily suspensions and oily solutions, since if they were injected intravenously blockage of small blood vessels might occur leading to poor vascular supply of local tissues possibly resulting in gangrene.

Intravascular routes

These are either intra-arterial (into arteries) or intravenous (into veins). The intra-arterial route is used for an immediate effect in a peripheral organ, e.g. to improve circulation to the extremities when arterial flow is restricted by arterial spasm or early gangrene. Tolazoline hydrochloride, a peripheral vasodilator, is sometimes administered by this route.

Substances are introduced directly into the blood stream by the intravenous route. The most common site is the median basilic vein at the anterior surface of the elbow. The volume can vary from less than 1 ml to in excess of 500 ml. Small volumes may be administered for a rapid effect (e.g. anaesthetics) and large volumes (perfusion or infusion fluids) to replace body fluid loss in shock, severe burns, vomiting and diar-

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