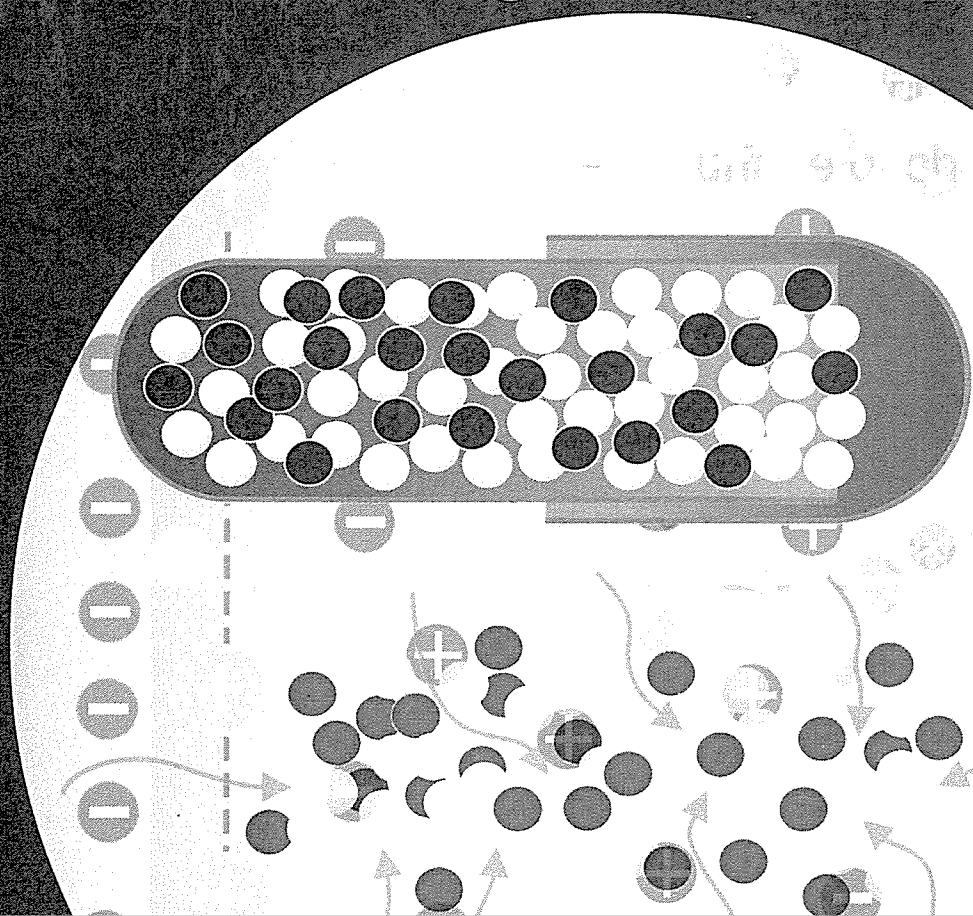


Pharmaceutics

The science of dosage form design

Edited by
M. E. Aulton



Pharmaceutics

The Science of Dosage Form Design


Edited by

Michael E. Aulton BPharm PhD MRPharmS

Professor of Pharmaceutical Technology, De Montfort University, Leicester, UK



CHURCHILL LIVINGSTONE
An imprint of Harcourt Publishers Limited

 is a registered trademark of Harcourt Publishers Limited

© Michael Aulton 1988

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form by any means, electronic, mechanical, photocopying, recording or otherwise, without either the prior permission of the publishers (Harcourt Publishers Limited, 24–28 Oval Road, London NW1 7DX), or a licence permitting restricted copying in the United Kingdom issued by the Copyright Licensing Agency Ltd, 90 Tottenham Court Road, London W1P 0LP.

First published 1988

Reprinted 1989

Reprinted 1990

Reprinted 1991

Reprinted 1992

Reprinted 1994 (twice)

Reprinted 1995

Reprinted 1996 (twice)

Reprinted 1998

Reprinted 2000

ISBN 0-443-03643-8

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

Library of Congress Cataloging in Publication Data

A catalog record is available from the Library of Congress

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

Mixing

THEORY OF MIXING

Types of mixtures

The mixing process

The scale of scrutiny

Degree of mixing

THE MIXING OF POWDERED MATERIALS

Mechanisms of mixing — convective, shear and diffusive mixing

Influence of powder aggregates on mixing

Segregation (demixing)

Types of segregation

Percolation segregation

Trajectory segregation

Densification segregation

Effect of mixing time on segregation

Ordered mixing

The practical importance of ordered mixing

Segregation of ordered mixes

Ordered unit segregation

Displacement segregation

Saturation segregation

Industrial powder mixers

Tumbling mixers

Agitator mixers

High speed granulators

Scale-up of powder mixing

THE MIXING OF MISCIBLE LIQUIDS AND SUSPENSIONS

Propeller mixers

Turbine mixers

In-line mixers

THE MIXING OF SEMISOLIDS

Mixers for semisolids

The planetary mixer

The sigma blade mixer

Mixing may be defined as a process where two or more components are treated so as to lie as nearly as possible in contact with a particle of each of the other components. The aim of the process is to produce one of the following:

- 1 a blend of solid particles (powder mixing),
- 2 a suspension of an insoluble solid in a liquid,
- 3 a mixture of miscible liquids,
- 4 a dispersion of particles in a semisolid as in the preparation of ointments or pastes.

A mixing stage is involved at some time in the preparation of practically every pharmaceutical preparation.

THEORY OF MIXING

Types of mixtures

Miscible liquids, gases and vapours will in time completely mix spontaneously by diffusion and no energy need be used for this to occur. This *positive mixing* may be contrasted with the *negative mixing* of insoluble solid particles with a liquid where the particles will separate out unless work is done by stirring to keep them dispersed. A mixture of powdered constituents is an example of a *neutral mix*. Work must be done to mix them initially but usually there is then no tendency for demixing to occur spontaneously; though demixing is possible in certain circumstances.

The mixing process

To simplify discussion the principles of mixing will be considered by reference to a system consisting of *equal* quantities of two constituents

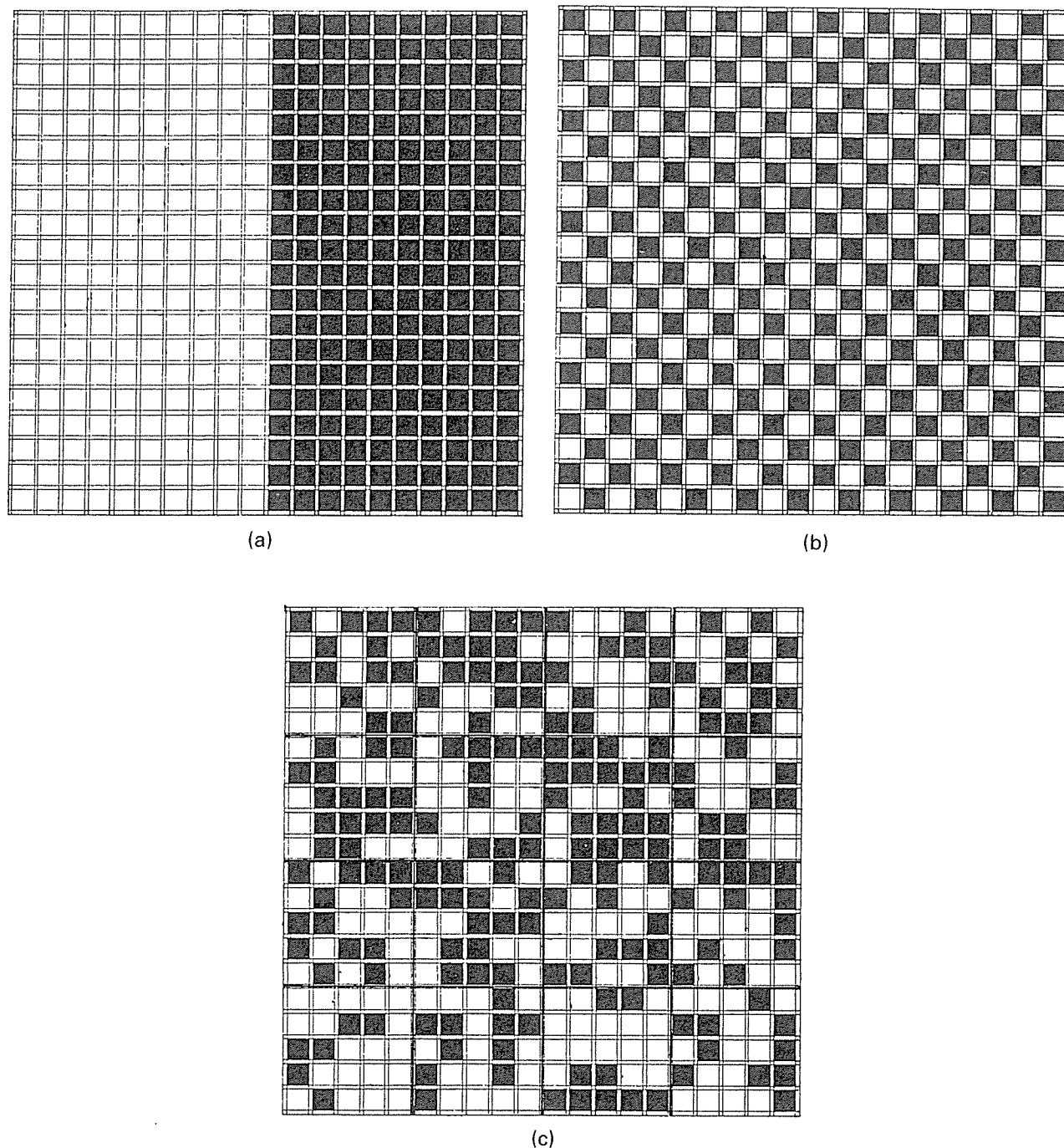


Fig. 32.1 Powder mixing: (a) segregated particles (b) ideal mixing (c) random mixing

A and B of the same size and shape though those conditions are rarely found in practice.

The process can be represented by representing the materials as filled and open squares in Fig. 32.1. Fig. 32.1(a) shows the particles in a completely segregated state prior to mixing. As mixing proceeds it is just conceivable that a so-called *perfect* mix may be produced where each

component (Fig. 32.1(b)). The odds against this happening are so great that the best attainable mix will actually be a *random mix* represented by Fig. 32.1(c). A random mix may be defined as one where the probability of sampling a particular type of particle is proportional to the number of such particles on the total mix. In a large number of trials where single particles were withdrawn there would be equal numbers of each type

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.