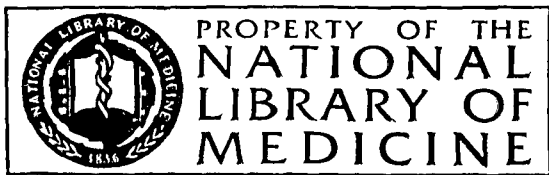


NATIONAL LIBRARY OF MEDICINE

**Physicochemical
Principles
of Pharmacy** **Third Edition**

A. T. Florence



PHYSICOCHEMICAL PRINCIPLES OF PHARMACY

A. T. FLORENCE

*The School of Pharmacy
University of London*

and

D. ATTWOOD

*School of Pharmacy and Pharmaceutical Sciences
University of Manchester*

THIRD EDITION





© A. T. Florence and D. Attwood 1981, 1988, 1998

All rights reserved. No reproduction, copy or transmission of this publication may be made without written permission.

No paragraph of this publication may be reproduced, copied or transmitted save with written permission or in accordance with the provisions of the Copyright, Designs and Patents Act 1988, or under the terms of any licence permitting limited copying issued by the Copyright Licensing Agency, 90 Tottenham Court Road, London W1P 9HE.

Any person who does any unauthorised act in relation to this publication may be liable to criminal prosecution and civil claims for damages.

The authors have asserted their rights to be identified as the authors of this work in accordance with the Copyright, Designs and Patents Act 1988.

First published 1981 by
MACMILLAN PRESS LTD
Houndmills, Basingstoke, Hampshire RG21 6XS
and London
Companies and representatives
throughout the world

First edition 1981
Second edition 1988
Third edition 1998

ISBN 0-333-69081-8

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

This book is printed on paper suitable for recycling and
made from fully managed and sustained forest sources.

10 9 8 7 6 5 4 3 2 1
07 06 05 04 03 02 01 00 99 98

Typeset in Great Britain by
Aarontype Limited
Easton, Bristol

Printed and bound in Great Britain by
Creative Print & Design (Wales), Ebbw Vale

Coems Ex 2042 p. 4

Contents

| | |
|---|-----------|
| <i>Preface</i> | <i>x</i> |
| <i>Acknowledgements</i> | <i>xi</i> |
| Introduction | 1 |
| 1 Properties of the Solid State | 5 |
| 1.1 Crystal structure | 5 |
| 1.2 Crystal form | 8 |
| 1.2.1 Crystallisation and factors affecting crystal form ² | 9 |
| 1.3 Polymorphism | 11 |
| 1.3.1 Pharmaceutical implications of polymorphism | 14 |
| 1.4 Crystal hydrates | 18 |
| 1.4.1 Pharmaceutical consequences of solvate formation | 18 |
| 1.5 Dissolution of solid drugs | 21 |
| 1.6 Biopharmaceutical importance of particle size | 22 |
| 1.7 Wetting of powders | 26 |
| 1.7.1 Contact angle and wettability of solid surfaces | 27 |
| 1.7.2 Wettability of powders | 28 |
| 1.8 Solid dispersions | 29 |
| 1.8.1 Eutectics and drug identification | 32 |
| 1.9 Summary | 33 |
| 2 Gases and Volatile Agents | 36 |
| 2.1 Pressure units | 36 |
| 2.2 Ideal and non-ideal gases | 36 |
| 2.3 Vapour pressure | 38 |
| 2.3.1 Vapour pressure and solution composition: Raoult's law | 38 |
| 2.3.2 Variation of vapour pressure with temperature: Clausius-Clapeyron equation | 41 |
| 2.3.3 Vapour pressure lowering | 44 |
| 2.4 Solubility of gases in liquids | 46 |
| 2.4.1 Effect of temperature on solubility | 47 |
| 2.4.2 Effect of pressure on solubility | 47 |
| 2.4.3 The solubility of volatile anaesthetics in oil | 49 |
| 2.5 The solubility of gases in blood and tissues | 50 |
| 2.5.1 The solubility of oxygen in blood | 50 |
| 2.5.2 The solubility of anaesthetic gases in blood and tissues | 51 |
| 2.6 Summary | 54 |
| 3 Physicochemical Properties of Drugs in Solution | 56 |
| 3.1 Concentration units | 56 |
| 3.1.1 Weight concentration | 56 |
| 3.1.2 Molarity and molality | 56 |
| 3.1.3 Milliequivalents | 57 |

GILSHS AP BLK 780625

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.