

**SECOND EDITION**

---

**Chemical Stability  
of Pharmaceuticals**

---

**A HANDBOOK FOR PHARMACISTS**

---

**Kenneth A. Connors  
Gordon L. Amidon  
Valentino J. Stella**

**Chemical Stability  
of Pharmaceuticals**

---

**A Handbook for Pharmacists**

**Second Edition**

**Kenneth A. Connors**

School of Pharmacy, The University of Wisconsin

**Gordon L. Amidon**

College of Pharmacy, The University of Michigan

**Valentino J. Stella**

School of Pharmacy, The University of Kansas

A Wiley-Interscience Publication

**JOHN WILEY & SONS**

New York • Chichester • Brisbane • Toronto • Singapore

**A NOTE TO THE READER**

This book has been electronically reproduced from digital information stored at John Wiley & Sons, Inc. We are pleased that the use of this new technology will enable us to keep works of enduring scholarly value in print as long as there is a reasonable demand for them. The content of this book is identical to previous printings.

Copyright © 1986 by John Wiley & Sons, Inc.

All rights reserved. Published simultaneously in Canada.

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except as permitted under Sections 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher, or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400, fax (978) 750-4470. Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, (201) 748-6011, fax (201) 748-6008.

**Library of Congress Cataloging in Publication Data:**

Connors, Kenneth A. (Kenneth Antonio), 1932-  
Chemical stability of pharmaceuticals.

"A Wiley-Interscience publication."

Includes bibliographies and index.

1. Drug stability. I. Amidon, Gordon L. II. Stella, Valentino J., 1946- . III. Title. [DNLM: 1. Drug Stability—handbooks. 2. Kinetics—handbooks. QV 735 C752c]

RS424.C66 1986 615'.18 85-31455  
ISBN 0-471-87955-X

Printed in India

10 9 8 7 6 5 4 3

To the memory of Lloyd Kennon

v

## Preface

Pharmaceutics instruction in the pharmacy curriculum provides pharmacists with (among other kinds of knowledge) a sound theoretical basis for understanding chemical kinetics and its uses in studying drug stability. This is a research application of kinetics in pharmacy, and it is entirely appropriate that the pharmacist be aware of the methods used (primarily in the pharmaceutical industry) to assess and control drug and dosage form stability. There is, however, another area of pharmacy in which a knowledge of kinetics can be usefully applied: this is the area of professional practice. Teachers of pharmaceutics have not been highly successful, it seems to us, in developing this application. The purpose of this book is to assist the pharmacist in applying kinetic methods and data to stability problems in professional practice.

The way from theory to practice is not always easy or obvious. Part One of this book treats the calculations, approximations, and estimates that are useful in practical situations. Part Two is a collection of selected drug-stability data from the literature. Although it is clearly not encyclopedic, this collection makes readily accessible to the pharmacist much of the information necessary to make pharmaceutical decisions about drug stability. It has been interesting to learn, in the several years since the first edition appeared, that research pharmacists in the pharmaceutical industry also have found the book useful, primarily because of the data presented in the stability monographs.

In this second edition the principal changes are a thorough revision of the chapter on oxidation, addi-

# 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.