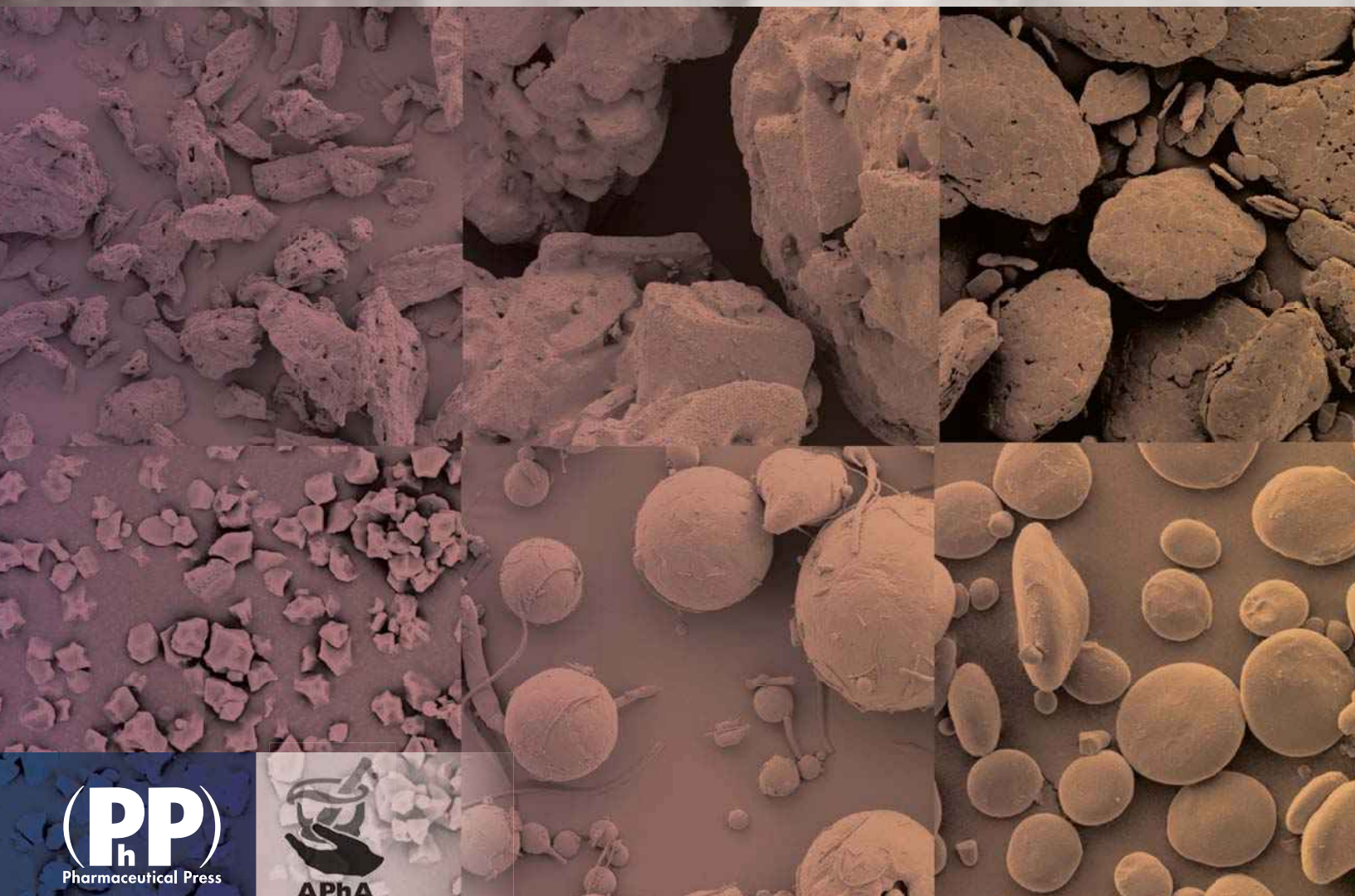


Handbook of Pharmaceutical Excipients

Sixth edition

Edited by
Raymond C Rowe, Paul J Sheskey and Marian E Quinn



PP
Pharmaceutical Press



DOCKET
A L A R M

Find authenticated court documents without watermarks at docketalarm.com.

Handbook of Pharmaceutical Excipients

SIXTH EDITION

Edited by

Raymond C Rowe BPharm, PhD, DSC, FRPharmS, FRSC, CPhys, MInstP

Chief Scientist

Intelligensys Ltd, Stokesley, North Yorkshire, UK

Paul J Sheskey BSc, RPh

Application Development Leader

The Dow Chemical Company, Midland, MI, USA

Marian E Quinn BSc, MSc

Development Editor

Royal Pharmaceutical Society of Great Britain, London, UK



Published by the Pharmaceutical Press

An imprint of RPS Publishing

1 Lambeth High Street, London SE1 7JN, UK
100 South Atkinson Road, Suite 200, Grayslake, IL 60030-7820, USA

and the American Pharmacists Association

2215 Constitution Avenue, NW, Washington, DC 20037-2985, USA

© Pharmaceutical Press and American Pharmacists Association 2009

(PP) is a trade mark of RPS Publishing

RPS Publishing is the publishing organisation of the Royal Pharmaceutical Society of Great Britain

First published 1986
Second edition published 1994
Third edition published 2000
Fourth edition published 2003
Fifth edition published 2006
Sixth edition published 2009

Typeset by Data Standards Ltd, Frome, Somerset
Printed in Italy by L.E.G.O. S.p.A.

ISBN 978 0 85369 792 3 (UK)
ISBN 978 1 58212 135 2 (USA)

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, without the prior written permission of the copyright holder.

The publisher makes no representation, express or implied, with regard to the accuracy of the information contained in this book and cannot accept any legal responsibility or liability for any errors or omissions that may be made.

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

14 Safety

Hydrogenated castor oil is used in oral and topical pharmaceutical formulations and is generally regarded as an essentially nontoxic and nonirritant material.

Acute oral toxicity studies in animals have shown that hydrogenated castor oil is a relatively nontoxic material. Irritation tests with rabbits show that hydrogenated castor oil causes mild, transient irritation to the eye.

LD₅₀ (rat, oral): >10 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16 Regulatory Status

Accepted in the USA as an indirect food additive. Included in the FDA Inactive Ingredients Database (oral capsules, tablets, and sublingual tablets).

Included in nonparenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

17 Related Substances

Castor oil; vegetable oil, hydrogenated.

18 Comments

Various different grades of hydrogenated castor oil are commercially available, the composition of which may vary considerably.

Sterotex K (Karlshamns Lipid Specialities), for example, is a mixture of hydrogenated castor oil and hydrogenated cottonseed oil. See Vegetable Oil, hydrogenated for further information.

The EINECS number for hydrogenated castor oil is 232-292-2.

19 Specific References

- 1 Kline CH. Thixcin R-thixotrope. *Drug Cosmet Ind* 1964; 95(6): 895–897.
- 2 Yonezawa Y *et al.* Release from or through a wax matrix system. III: Basic properties of release through the wax matrix layer. *Chem Pharm Bull (Tokyo)* 2002; 50(6): 814–817.
- 3 Vergote GJ *et al.* An oral controlled release matrix pellet formulation containing microcrystalline ketoprofen. *Int J Pharm* 2002; 219: 81–87.
- 4 Danish FQ, Parrott EL. Effect of concentration and size of lubricant on flow rate of granules. *J Pharm Sci* 1971; 60: 752–754.
- 5 Hölzer AW, Sjögren J. Evaluation of some lubricants by the comparison of friction coefficients and tablet properties. *Acta Pharm Suec* 1981; 18: 139–148.

20 General References

—

21 Author

RT Guest.

22 Date of Revision

11 February 2009.

Cellulose, Microcrystalline

1 Nonproprietary Names

BP: Microcrystalline Cellulose

JP: Microcrystalline Cellulose

PhEur: Cellulose, Microcrystalline

USP-NF: Microcrystalline Cellulose

2 Synonyms

Avicel PH; *Celllets*; *Celex*; cellulose gel; hellulosum microcrystallinum; *Celphere*; *Ceolus KG*; crystalline cellulose; E460; *Emcocel*; *Ethispheres*; *Fibrocel*; *MCC Sanaq*; *Pharmacel*; *Tabulose*; *Vivapur*.

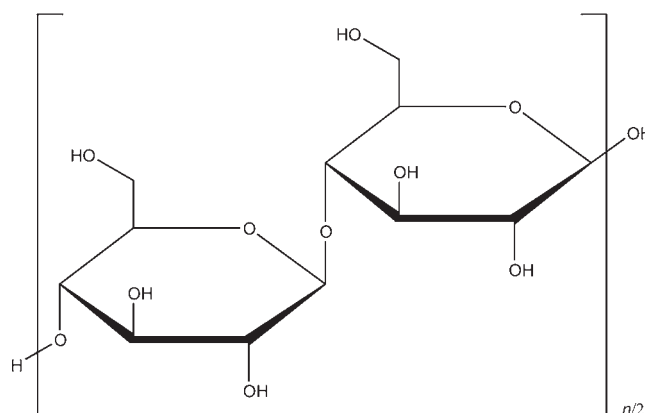
3 Chemical Name and CAS Registry Number

Cellulose [9004-34-6]

4 Empirical Formula and Molecular Weight

(C₆H₁₀O₅)_n ~36,000

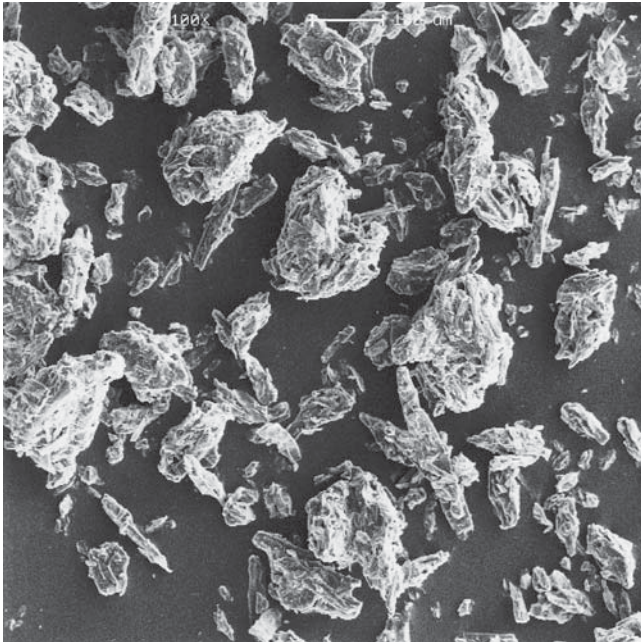
5 Structural Formula



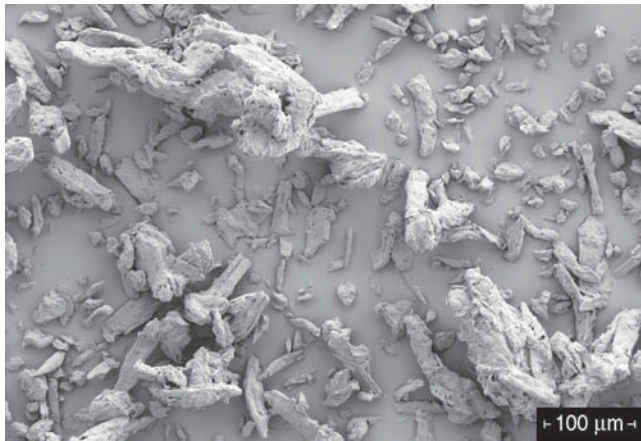
6 Functional Category

Adsorbent; suspending agent; tablet and capsule diluent; tablet

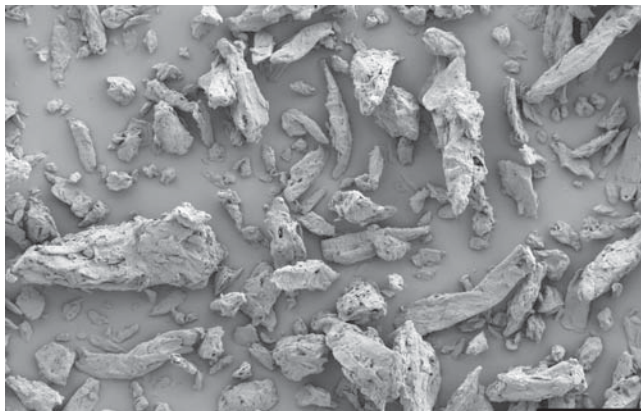
SEM 1: Excipient: microcrystalline cellulose; manufacturer: JRS Pharma LP; lot no.: 98662; magnification: 100×.



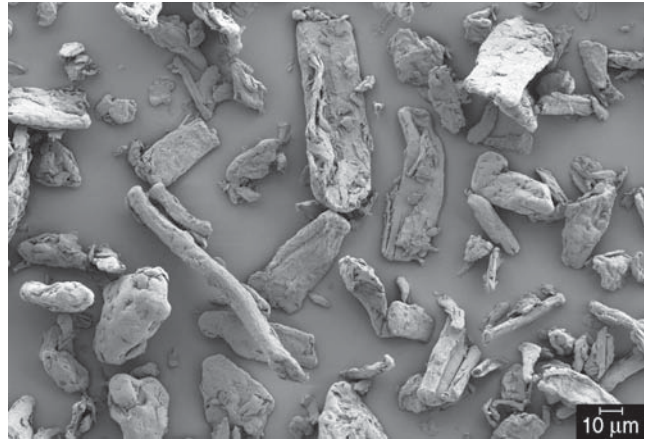
SEM 2: Excipient: microcrystalline cellulose (*Avicel PH-101*); manufacturer: FMC Biopolymer. magnification: 200×; voltage: 3 kV.



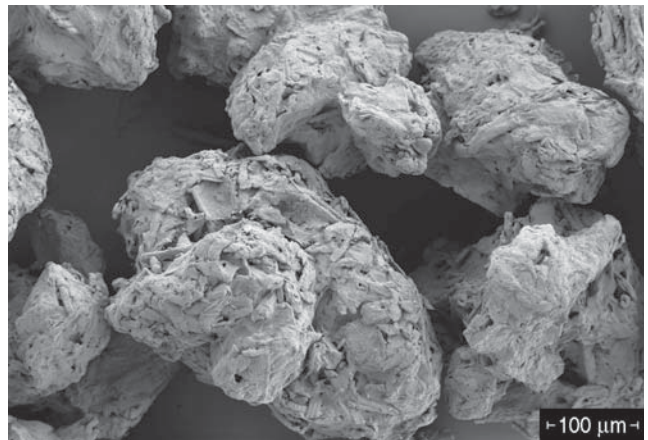
SEM 3: Excipient: microcrystalline cellulose (*Avicel PH-102*); manufacturer: FMC Biopolymer. magnification: 200×; voltage: 3 kV.



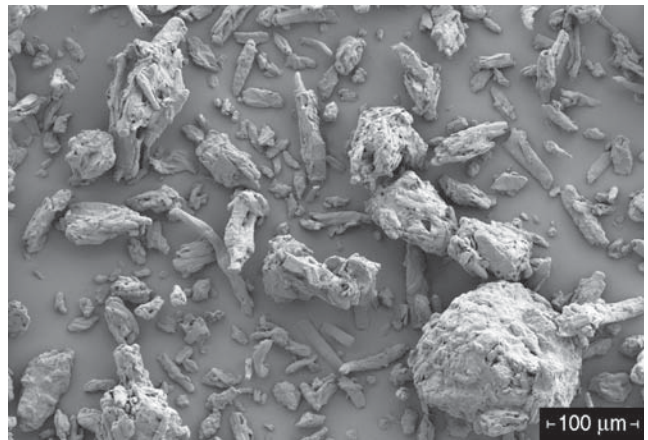
SEM 4: Excipient: microcrystalline cellulose (*Avicel PH-105*); manufacturer: FMC Biopolymer. magnification: 500×; voltage: 3 kV.



SEM 5: Excipient: microcrystalline cellulose (*Avicel PH-200*); manufacturer: FMC Biopolymer. magnification: 200×; voltage: 3 kV.



SEM 6: Excipient: microcrystalline cellulose (*Avicel PH-302*); manufacturer: FMC Biopolymer. magnification: 200×; voltage: 3 kV.



7 Applications in Pharmaceutical Formulation or Technology

Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder/diluent in oral tablet and capsule formulations where it is used in both wet-granulation and direct-compression processes.⁽¹⁻⁷⁾ In addition to its use as a binder/diluent, microcrystalline cellulose also has some lubricant⁽⁸⁾ and disintegrant

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.