
Handbook of PHARMACEUTICAL EXCIPIENTS

Third Edition

Edited by

Arthur H. Kibbe, Ph.D.

Professor and Chair
Department of Pharmaceutical Sciences
Wilkes University School of Pharmacy
Wilkes-Barre, Pennsylvania



American Pharmaceutical Association
Washington, D.C.



London, United Kingdom

Published by the American Pharmaceutical Association
2215 Constitution Avenue NW, Washington, DC 20037-2985, USA
www.aphanet.org
and the Pharmaceutical Press
1 Lambeth High Street, London SE1 7JN, UK
www.pharmpress.com

© 1986, 1994, 2000 American Pharmaceutical Association and Pharmaceutical Press

First edition 1986
Second edition 1994
Third edition 2000

Printed in the United States of America

ISBN: 0-85369-381-1 (UK)
ISBN: 0-917330-96-X (USA)

Library of Congress Cataloging-in-Publication Data

Handbook of pharmaceutical excipients / edited by Arthur H. Kibbe.--3rd ed.
p. ; cm.

Includes bibliographical references and index.

ISBN 0-917330-96-X

1. Excipients--Handbooks, manuals, etc. I. Kibbe, Arthur H. II. American
Pharmaceutical Association.

[DNLM: 1. Excipients--Handbooks. QV 735 H236 2000]

RS201.E87 H36 2000

615'.19--dc21

99-044554

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

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.

Managing Editor: Melanie Segala
Copyeditor: Paul Gottehrer
Indexer: Lillian Rodberg
Compositor: Roy Barnhill
Cover Designer: Tim Kaage

Polyethylene Oxide

1. Nonproprietary Names

USP: Polyethylene oxide

2. Synonyms

Polyox; polyoxirane; polyoxyethylene.

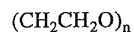
3. Chemical Name and CAS Registry Number

Polyethylene oxide [25322-68-3]

4. Empirical Formula Molecular Weight

See Table I.

5. Structural Formula



Polyethylene oxide is a nonionic homopolymer of ethylene oxide, where n represents the average number of oxyethylene groups (about 2000 to over 100 000). It may contain up to 3% of silicon dioxide.

6. Functional Category

Hydrophilic matrix formation; mucoadhesive; tablet binder; thickening agent.

7. Applications in Pharmaceutical Formulation or Technology

Polyethylene oxide can be used as a tablet binder at concentrations from 5-85%. The higher molecular weight grades provide delayed drug release via the hydrophilic matrix approach. Fig. 1 presents the relationship between swelling capacity and molecular weight which is a good guide when selecting products for use in immediate- or sustained-release matrix formulations.

Polyethylene oxide has been shown to be an excellent mucoadhesive polymer.⁽¹⁾ Low levels of polyethylene oxide are effective thickeners, although alcohol is usually added to water-based formulations to provide improved viscosity stability. Polyethylene

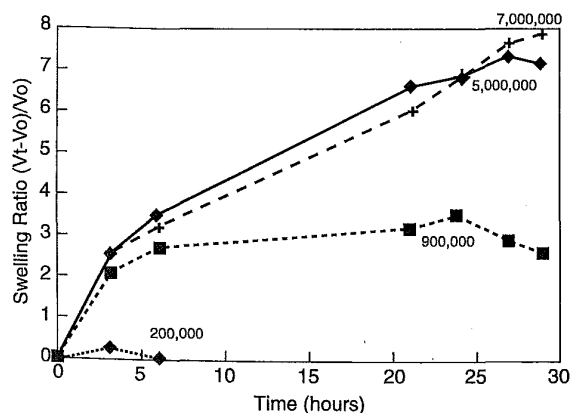


Fig. 1: Swelling capacity of polyethylene oxide (Polyox WSR). Measured for four molecular weight grades; 28 mm tablets in 300 mL of water.

oxide films demonstrate good lubricity when wet. This property has been utilized in the development of coatings for medical devices. Polyethylene oxide can be radiation crosslinked in solution to produce a hydrogel. The hydrogels so produced have been used in wound-care applications.

Table I: Number of repeat units and molecular weight as a function of polymer grade.

Polyox grade	Approximate number of repeating units	Approximate molecular weight
WSR N-10	2275	100 000
WSR N-80	4500	200 000
WSR N-750	6800	300 000
WSR N-3000	9100	400 000
WSR 205	14 000	600 000
WSR 1105	20 000	900 000
WSR N-12K	23 000	1 000 000
WSR N-60K	45 000	2 000 000
WSR 301	90 000	4 000 000
WSR Coagulant	114 000	5 000 000
WSR 303	159 000	7 000 000

Note: Molecular weight based on dilute viscosity measurements.

Table II: Polyethylene oxide viscosity at 25°C (mPa s).

Polyox grade	5% solution	2% solution	1% solution
WSR N-10	30-50	—	—
WSR N-80	65-115	—	—
WSR N-750	600-1200	—	—
WSR N3000	2250-4500	—	—
WSR 205	4500-8800	—	—
WSR 1105	8800-17 600	—	—
WSR N-12K	—	400-800	—
WSR N-60K	—	2000-4000	—
WSR 301	—	—	1500-5500
WSR coagulant	—	—	5500-7500
WSR 303	—	—	7500-10 000

Note: All solution concentrations are based on the water content of the hydro-alcoholic solutions.

8. Description

White to off-white, free-flowing powder. Slight ammoniacal odor.

9. Pharmacopeial Specifications

Test	USP
Identification	+
Loss on drying (105°C for 45 min)	≤ 1%
Nonsilicon dioxide loss on ignition	≤ 2%
Silicon dioxide	≤ 3%
Heavy metals	≤ 0.001%
Free ethylene oxide	≤ 10 ppm
Organic volatile impurities	+
Trichloroethylene	≤ 100 ppm
Viscosity	+

10. Typical Properties

Angle of repose: 34°

Density (true): 1.3 g/cc

Melting point: 65-70°C

Moisture content: < 1%. See also Fig. 2.

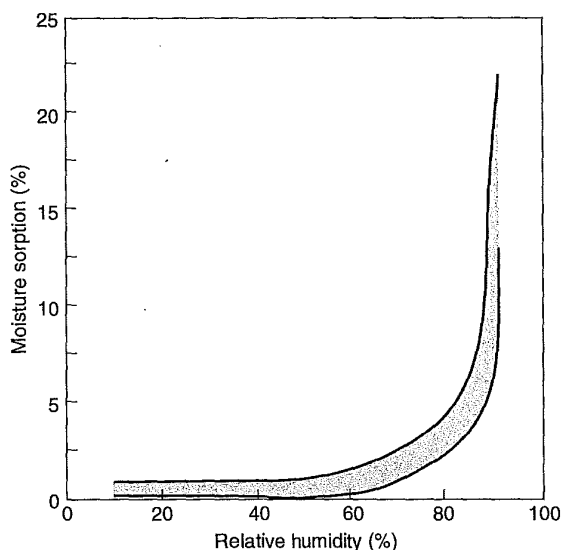


Fig. 2: Moisture sorption isotherm for polyethylene oxide (Polyox WSR), (Union Carbide Corp.)

Solubility: polyethylene oxide is soluble in water and a number of common organic solvents such as acetonitrile, chloroform, and methylene chloride. It is insoluble in aliphatic hydrocarbons, ethylene glycol, and most alcohols.⁽²⁾

11. Stability and Storage Conditions

Store in tightly sealed containers in a cool, dry, place. Avoid exposure to high temperatures since this can result in viscosity reduction.

12. Incompatibilities

Polyethylene oxide is incompatible with strong oxidizing agents.

13. Method of Manufacture

Prepared by the polymerization of ethylene oxide using a suitable catalyst.⁽²⁾

14. Safety

Animal studies suggest that polyethylene oxide has a low level of toxicity regardless of the route of administration. It is poorly absorbed from the gastrointestinal tract but appears to be completely and rapidly eliminated. The resins are neither skin irritants nor sensitizers, nor do they cause eye irritation.⁽⁶⁾

15. Handling Precautions

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

16. Regulatory Status

Included in the FDA Inactive Ingredients Guide (sustained-release tablets).

17. Pharmacopeias

US.

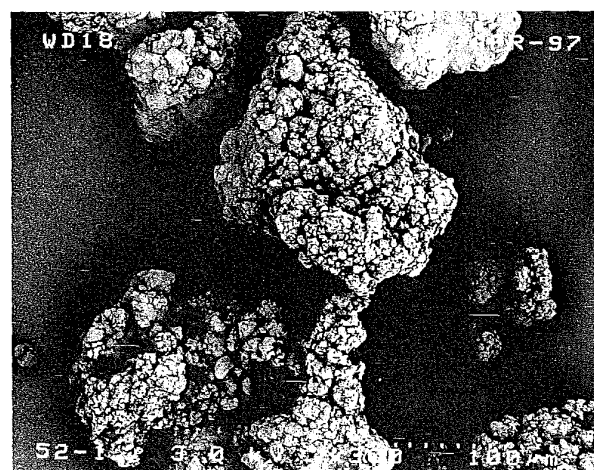
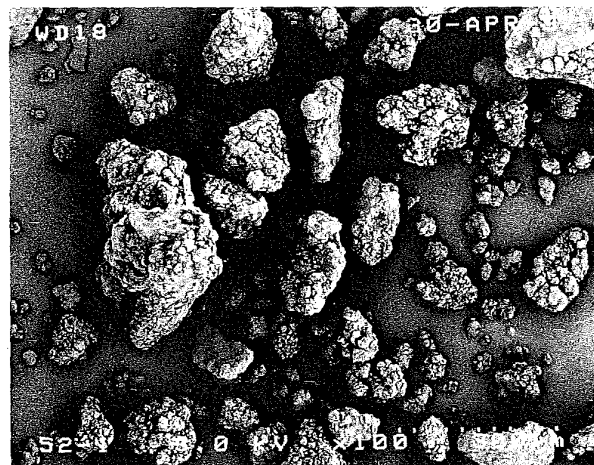


Fig. 3: SEM of polyethylene oxide (Polyox WSR), (Union Carbide Corp.). Magnifications at 100x (top) and 300x (bottom).

18. Related Substances

Polyethylene glycol.

19. Comments

—

20. Specific References

1. Bottenberg P, et al. Development and testing bioadhesive. *J Pharm Pharmacol* 1991; 43: 457-464.
2. Bailey FE Jr., Kolesky JV. *Poly(ethylene oxide)*. London, Academic Press, 1976.

21. General References

- Union Carbide Corp. Technical Literature: *Polyox* water soluble resin, 1998.
- Yu DM, Amidon GL, Weiner ND, Goldberg AH. Viscoelastic properties of poly(ethylene oxide) solution. *J Pharm Sci* 1994; 83: 1443-1449

22. Author

RL Schmitt.

- HFC 152a, 184
HFC (difluoroethane), 184
High fructose syrup, 211
HMCP, 256
Hodag *GMO*, 223
Hodag *GMS*, 225
Hodag *PEG*, 392
Hodag *SML*, 511
Hodag *SMO*, 511
Hodag *SMP*, 511
Hodag *SMS*, 511
Hodag *SSO*, 511
Hodag *STS*, 511
Hog gum (caramania), 569
Homopolymer ethenol, 424
Homopolymer 1-ethenyl-2-pyrrolidinone, 433
HPMC, 252
HSA, 5
Human serum albumin, 5
Human serum albumin, normal, 5
Humectants
 glycerin, 220
 propylene glycol, 442
 sorbitol, 515
 triacetin, 570
Hyamine 3500, 33
Hydrated aluminum silicate, 269
Hydrate sodium propanoate, 498
Hydrate sodium propionate, 498
Hydrate sodium salt, 498
Hydrocarbons (HC), 236
Hydrochloric acid, 239
Hydrogenated
 castor oil, 92, 579
 cottonseed oil, 578
 glucose syrup, 315
 maltose, 313
 oil, 578
 palm oil, 578
 polyoxyl castor oil, 412
 soybean oil, 578
 vegetable glycerides, 550
 vegetable oil
 type I, 157, 578
 type II, 579
Hydrogen 1,2-benzenedicarboxylate
 2-hydroxypropyl methyl ether, 256
Hydrogen 1,2-benzenedicarboxylate, 99
Hydrogen carbonate, 476
Hydrogen orthophosphate, dipotassium, 494
Hydrogen phosphate, disodium, 493
Hydrogen sulfite, 491
 α -Hydro- ω -hydroxy-poly(oxy-1,2-ethanediyl), 392
 α -Hydro- ω -
 hydroxypoly(oxyethylene)poly(oxypropylene)poly(oxyethylene) block copolymer, 386
2-Hydroperfluoropropane, 234
Hydrophilic matrix formation
 polyethylene oxide, 399
Hydrous lanolin, 287, 289, 290
Hydrous wool fat, 290
Hydroxyapatite, 68
Hydroxybenzene, 367
4-Hydroxybenzoic acid butyl ester, 53
4-Hydroxybenzoic acid ester, 340
4-Hydroxybenzoic acid ethyl ester, 205
4-Hydroxybenzoic acid propyl ester, 450
Hydroxybutanedioic acid, 311
2-Hydroxy-1,4-butanedioic acid, 311
(RS)-(±)-Hydroxybutanedioic acid, 311
1-Hydroxy-1,2-ethanecarboxylic acid, 311
4-Hydroxy-3-ethoxybenzaldehyde, 208
 β -Hydroxyethylamine, 350
2-Hydroxyethylamine, 350
 β -Hydroxyethyl benzene, 372
Hydroxyethyl cellulose, 240, 248, 254
Hydroxyethylcellulosum, 240
2-Hydroxyethyl- β -cyclodextrin, 167
Hydroxyethyl ether, 240
2-Hydroxyethyl ether, 240
 β -Hydroxyethyl phenyl alcohol, 370
 β -Hydroxyethyl phenyl ether, 370
3-Hydroxy-2-ethyl-4-pyrone, 201
4-Hydroxy-*m*-anisaldehyde, 576
4-Hydroxy-2-methoxybenzaldehyde, 576
3-Hydroxy-2-methyl-4*H*-pyran-4-one, 320
N-(Hydroxymethyl)-*N*-(1,3-dihydroxymethyl-2,5-dioxo-4-imidazolidinyl)-*N'*-(hydroxymethyl)urea, 262
3-Hydroxy-2-methyl-(1,4-pyran), 320
3-Hydroxy-2-methyl-4-pyrone, 320
p-Hydroxy-*m*-methoxybenzaldehyde, 576
1-Hydroxy-2-phenoxyethane, 370
2-Hydroxy-1,2,3-propanetricarboxylic acid, triethyl ester, 573
2-Hydroxypropane-1,2,3-tricarboxylic acid monohydrate, 140
2-Hydroxy-1,2,3-propanetricarboxylic acid tripotassium salt monohydrate, 429
2-Hydroxy-1,2,3-propanetricarboxylic acid monohydrate, 140
1-Hydroxypropanol, 442
 α -Hydroxypropionic acid, 272
2-Hydroxypropionic acid, 272
(R)-(-)-2-Hydroxypropionic acid, 272
(S)-(+)-2-Hydroxypropionic acid, 272
Hydroxypropyl alginate, 445
Hydroxypropyl cellulose, 243, 244, 250, 254
 low-substituted, 248, 249
Hydroxypropylcellulosum, 244
2-Hydroxypropyl- β -cyclodextrin, 167
3-Hydroxypropyl- β -cyclodextrin, 167
Hydroxypropyl ether, 244
2-Hydroxypropyl ether, 244
 low-substituted, 249
Hydroxypropyl methylcellulose, 243, 248, 252, 259, 338
Hydroxypropyl methylcellulose phthalate, 100, 254, 256
2-Hydroxypropyl methylcellulose phthalate, 256
Hydroxypropyl methyl ether, 252
2-Hydroxypropyl methyl ether, 252
2-Hydroxysuccinic acid, 311
Hydroxytoluene, 50, 158
Hy-Phi, 356
Hyprolose, 244
HyQual, 608
Hystrene, 534
Icing sugar, 546
Idroramnosan, 240
Imidazolidinyl urea, 261
Imidurea, 261
2,2'-Iminobisethanol, 180
2,2'-Iminodiethanol, 180
Imwitor 191, 225
Imwitor 900K, 225
Indanthrene blue (D&C blue #9), 147
Indices
 Bonding Index (BI), 637
 Brittle Fracture Index (BFI), 637
Indigo carmine, 146, 151
Indigotine (FD&C blue #2), 147
Indigotine (FD&C blue #4 lake), 148
Industrene, 356, 534
Industrial methylated spirit, 8
Instastarch, 528
Instrumentation, 636
Invert sugar, 543
IPA, 263
Irish moss extract, 91
Iron oxide coloring agents, 146, 148, 150, 151
Iron oxides, synthetic, 149
Isceon 134a, 560
Isceon 142b, 132
Isobutane, 236
Isomyst, 265
6-Isooctadecanoate, 511
Isopal, 267
Isopalm, 267
Isopropanol, 263
Isopropyl alcohol, 8, 263
Isopropyl hexadecanoate, 267
Isopropylis myristas, 265
Isopropylis palmitas, 267
2-Isopropyl-5-methylcyclohexanol, 334
4-Isopropyl-1-methylcyclohexan-3-ol, 334
Isopropyl myristate, 265, 268
Isopropyl palmitate, 266, 267
Isotron, 134
Ja-Fa IPM, 265
Ja-Fa IPP, 267
Jaguar gum, 232
Jelly
 mineral, 362
 petroleum, 362
 yellow petroleum, 362
Jinjili oil, 460
Kalii chloridum, 426
Kalii citras, 429
Kalii hydrogencarbonas, 476
Kalii sorbas, 431
Kaolin, 32, 269, 298
Kaolinum ponderosum, 269
Kelacid, 10
Kelcoloid, 445
Keltone, 465
Kelcosol, 465
Keltrol, 599
Kemstrene, 220
Keoflo ADP, 531
Kessco 40, 225
Kessco EO, 203