Handbook of Pharmaceutical EXCIPIENTS

American Pharmaceutical Association

Handbook of PHARMACEUTICAL EXCIPIENTS

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Preface

Experienced pharmaceutical formulators have for many years needed a systematic and comprehensive English language data resource on excipients: the additives used to convert pharmacologically active compounds into dosage forms suitable for administration to patients. The *Handbook of Pharmaceutical Excipients* was carefully planned and written to meet this need. It should serve as a reliable and useful source of technical information on the relationship between properties of excipients and the quality of dosage forms.

This volume includes 145 monographs in a uniform format on excipients most widely used in the preparation of pharmaceutical dosage forms. The technical information on these excipients was assembled from a wide, international range of scientific publications covering the physical, chemical and biological properties of these important materials. Examples of these properties include bulk and tap density, particle size distribution, crystal form, heat of adsorption, specific surface area, solubility, melting or boiling range, flowability, surface tension, sorption and desorption, photostability, etc. In addition, the *Handbook* includes information on documented interactions between excipients (sometimes still described as inert) and drug substances. These interactions may indeed create problems affecting the efficacy, safety and stability of pharmaceutical preparations.

Interest in excipients and their properties has expanded from a research perspective in line with the growing importance of bioavailability and bioequivalence. Among the factors known to affect drug absorption, the current revision of the *United States Pharmacopeia/National Formulary* mentions "the diluents and excipients used in formulating the dosage form, including fillers, binders, disintegrating agents, lubricants, coatings, solvents, suspending agents, and dyes." Although the monographs in this *Handbook* list many of the known interactions of excipients with drug substances, many other such interactions may not have been reported in the literature. Formulators are therefore advised to exercise caution and to undertake experimental studies before initiating clinical studies, particularly when dealing with new drug substances.

After the publication in 1974 of the *Katalog pharmazeutischer Hilfsstoffe* (*Catalog of Pharmaceutical Excipients*), which contains German-language monographs for nearly 100 Swiss pharmacopeial and non-pharmacopeial excipients, the idea of an edition in English was raised by United States and United Kingdom pharmaceutical scientists. This possibility was discussed at the 20th Annual Meeting of the American Pharmaceutical Association's Academy of Pharmaceutical Sciences in 1976. The goals established at that time included a recommendation to publish a Handbook of Pharmaceutical Excipients in the English language, structured in a format similar to the Swiss *Katalog*.

Noted British academic and industrial pharmaceutical scientists were contacted, and with their enthusiastic support, the cooperation of The Pharmaceutical Society of Great Britain was obtained. Their Industrial Pharmacists' Group Committee with the staff of the Department of Pharmaceutical Sciences of The Pharmaceutical Society of Great Britain then began collaborating with the APhA Academy of Pharmaceutical Sciences in the planning and preparation of the *Handbook of Pharmaceutical Excipients*. Aware of the Swiss connection, the publishers of the *Handbook* acknowledge the assistance and encouragement provided by the publishers of the *Katalog pharmazeutischer Hilfsstoffe*, namely, Ciba-Geigy, Hoffmann-La Roche, and Sandoz Ltd. in allowing an English translation of the *Katalog* to be made and used as a basis for the expanded *Handbook*.

To help expedite the publishing plan, steering committees in the U.S.A. and the U.K. were established to select excipients already officially recognized in *USP/NF* and *BP/EP* as well as to recommend non-official excipients which met the predetermined requirements for inclusion in the *Handbook*. The Steering Committees recognized the critical importance of distinguishing between information not requiring laboratory testing or evaluation and those parameters requiring laboratory testing. Examples of the latter include density, bulk and tap volume, particle size distribution, moisture sorption and desorption isotherms, mechanical properties, surface tension, viscosity and certain other properties of highly specific importance.

Scientific direction of the Handbook Project in the U.S.A. was the responsibility of an 18-member committee representing five schools of pharmacy and ten pharmaceutical companies under the chairmanship of Jack Cooper and Zak T.Chowhan. In the United Kingdom, the Pharmaceutical Excipients Project was directed by a committee of five academic and industry pharmacists under the chairmanship of Robert F. Weir.

Each monograph in the *Handbook* is divided into 20 sections as follows:

1 Nonproprietary Names
2 Functional Category or Categories
3 Synonyms
4 Chemical Names and CAS Registry Number
5 Empirical Formula and Molecular Weight
6 Structural Formula
7 Commercial Availability
8 Method of Manufacture
9 Description
10 Pharmacopeial Specifications
11 Typical Properties
12 Stability and Storage Conditions
13 Incompatibilities
14 Safety
15 Handling Precautions
16 Regulatory Acceptance
17 Applications in Pharmaceutical Formulation or Technology
18 Related Substances
19 Comments
20 Specific References
USA: Authors and Reviewers
UK: Authors and Reviewers

A number of monographs are "group monographs" containing description and technical information on two or more excipients belonging to a specific chemical series such as polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates, and sorbitan esters. At the end of each monograph the author(s) and the reviewer(s) are acknowledged by * and **, respectively. Many of the monographs include scanning electron microphotographs taken at varying magnifications.

The compendial specifications for excipients with monographs in *USP XXI/NF XVI*, *BP* 1980, and *BP* Addenda 1982 and 1983 appear in Section 10. For details on pharmacopeial specifications which are currently applicable, the reader must refer to the latest revisions of the compendia as well as the latest addenda or supplements. Technical data from the APhA Academy of Pharmaceutical Sciences Handbook of Pharmaceutical Excipients Project which were generated between 1979 and 1980 by 34 laboratories representing pharmacy schools and pharmaceutical industry in the U.S.A. are summarized in Section 11 of the monograph. The Laboratory Methods used by these laboratories are summarized in Appendix II.

Completion of the Handbook Project will represent the results of years of work by numerous contributors who have provided invaluable experience in the compilation of the data in the

monographs, 30 of which came from The Pharmaceutical Society of Great Britain. A total of 150 pharmaceutical scientists representing academic and industrial pharmacy in the U.S. and the U.K. volunteered their efforts for which we are most grateful. We also wish to extend our sincere thanks to James C. Boylan and Ralph T. Shangraw for their assistance in reviewing and correcting the galley proofs in cooperation with the staff of the American Pharmaceutical Association, and to Ainley Wade of The Pharmaceutical Society of Great Britain for invaluable help in this connection.

The planning and implementation of the *Handbook of Pharmaceutical Excipients* was directed by the two Steering Committees in the USA and UK whose members are listed on page vii.

Notice to Readers

1. The *Handbook of Pharmaceutical Excipients* is a compilation of information obtained from the scientific literature, experiments as conducted by members of the APhA Academy of Pharmaceutical Sciences, and personal observations by authors of the individual monographs. The *Handbook* was written by volunteers from either the APhA Academy of Pharmaceutical Sciences or The Pharmaceutical Society of Great Britain. It is intended to be a convenient reference work generally descriptive of excipient products available at the time information for the *Handbook* was compiled. There is no intent, implied or otherwise, that any of the information contained within constitutes standards for the substances described. References are made in various monographs to the *USP/NF* and/or *BP/EP*. Diligent effort was made to use compendial information available as of January 1, 1985. However, since compendial monographs are frequently revised, the reader is urged to consult the most current compendium, or its supplement, for correct information.

2. During the preparation of the *Handbook of Pharmaceutical Excipients*, effort was made to determine all of the suppliers of the various excipients mentioned in the *Handbook*. This proved to be a very difficult task. The identification of known suppliers of an excipient product does not constitute an endorsement of the supplier or its product, and the lack of identification of any supplier of an excipient product is not intended to reflect adversely on that supplier or its product.

3. The data reported with regard to particular excipient products reflects only the results of testing of the particular batch or sample tested. The data reported may not necessarily be reflected in other batches or samples.

Table of Contents

Acacia

1. Nonproprietary Name

NF: Acacia
BP/EP: Acacia

2. Functional Categories

USP: Tablet binder; suspending and/or viscosity-increasing agent; emulsifying and/or solubilizing agent
Other: protective colloid

3. Synonyms

Gum acacia; gum arabic

4. Chemical Name and CAS Registry Number

Acacia [9000-01-5]

5. Empirical Formula

—

Molecular Weight

240,000 to 580,000

6. Structural Formula

—

7. Commercial Availability

USA

Brampton Co., J. W.
Colloides Naturels
Colony Imports & Export Corp.
Dormar Chemicals, Inc.
Indiana Botanic Gardens, Inc.
Ingredient Technology Corp. Flavor & Fragrance Div.
Ingredients International, Inc.
Dr. Madis Laboratories, Inc.
Meer Corp.
Neal & Co., M. F.
Paulaur Corp.
Ruger Chemical Co.
TIC Gums, Inc.

UK

Arthur Branwell & Co., Ltd.
Chemical Exchange (UK), Ltd.
Courtin & Warner, Ltd.
M. Hamburer & Sons, Ltd.
Impaq, Ltd.
John Kelly's, Ltd.
Kimpton Bros., Ltd.
L.J. Rickard, Ltd.
Steetley Chemicals, Ltd.
A.F. Suter & Co., Ltd.
Thew, Arnott & Co., Ltd.

8. Method of Manufacture

Acacia is obtained from trees of the genus *Acacia* which grow in the Sudan and the Senegal region of Africa. The Kordofan grade from *Acacia verek* is considered to be the most desirable. The bark of the tree is cut, and the exudate which appears is allowed to dry on the bark. The dried exudate is collected and graded. The material is then processed by removal of bark, sand and other particulate matter, followed by grading, sizing and blending to various specifications. The various types differ in mesh size, water-insoluble residue, solution color and clarity. A spray-dried form is also available.

9. Description

Thin flakes, spheroidal tears, or in powdered or granular form; white or yellowish-white color; odorless, and bland taste.

10. Pharmacopeial Specifications

	NF (Tears or Powder)	BP/EP (Powder)	BP/EP (Tears)
Botanic characteristics		+	+
Identification	+	+	+
Microbial limits	*Salmonella* NEG.	*E. coli* NEG	—
Water	≤15%	—	—
Total ash	≤4%	—	—
Acid-insoluble ash	≤0.5%	—	—
Sulfated ash	—	≤5%	≤5%
Insoluble residue	≤1.0%	≤0.5%	≤0.5%
Solubility	—	+	+
Loss on drying	—	≤15.0%	≤15.0%
Arsenic	≤3 ppm	—	—
Lead	≤0.001%	—	—
Heavy metals	≤0.004%	—	—
Starch & dextrin	+	+	+
Tannin-bearing gums	+	+	+
Agar & tragacanth	—	+	+
Agar & sterculia gum	—	+	+
Sucrose & fructose	—	+	+

11. Typical Properties

Academy HPE Laboratory Project Data

Method	Lab #	Results (%)
MC-1	5	10.75[a]
MC-1	5	12.54[b]
MC-1	5	3.92[c]

Suppliers: Penick[a]; EM Labs[b]; Fisher[c]

Solubility: Water: 1 g in 2.7 g; alcohol: insoluble; glycerin: 1 g in 20 ml; propylene glycol: 1 g in 20 ml
pH (5% solution): 4.5-5.0.
Specific gravity: 1.35-1.49.
Viscosity of solutions: Variable; depending upon the source of the material, processing, storage conditions, pH and the presence of salts. Prolonged heating of acacia solutions results in a decrease of viscosity due to depolymerization or to particle agglomeration. The solutions exhibit Newtonian behavior.

12. Stability and Storage Conditions

Stored in a tight container in a cool, dry place. Solutions are subject to bacterial or enzymatic degradation. Powdered acacia should be preserved in an air-tight container.

13. Incompatibilities

Alcohol, adrenaline, amidopyrine, bismuth subnitrate, borax, cresol, eugenol, ferric salts, morphine, phenol, physostigmine, tannins, thymol, sodium silicate and vanillin. Many salts reduce the viscosity of acacia solutions, while trivalent salts may initiate coagulation. Acacia solutions carry a negative charge, and will form coacervates with gelatin and other substances. In the preparation of emulsions, solutions of acacia are incompatible with soaps.

14. Safety

Acacia is recognized as safe for general use as a food additive by the FDA and the Joint FAO/WHO Expert Committee on Food Additives. Although generally recognized as free from adverse reactions following ingestion, there have been a limited number of reports of allergenic reactions in man. It is not for parenteral use due to the danger of arabinosis.

15. Handling Precautions

None

16. Regulatory Acceptance

NF XVI; BP/EP 1980

17. Applications in Pharmaceutical Formulation or Technology

Use	Concentration (%)
Emulsifying agent	5.0-10.0
Suspending agent	5.0-10.0
Table binder	1.0-5.0 (Caution must be exercised to avoid prolonged disintegration time)

18. Related Substances

None

19. Comments

None

20. Specific References

1. G. O. Aspinal, Gums and Mucilages, *Advances in Carbohydrate Chemistry and Biochemistry*, 24, 333-379 (1969).
2. R. L. Whistler, "Industrial Gums," Academic Press, New York, N.Y., 1959.
3. F. Smith and R. Montgomery, "The Chemistry of Plant Gums and Mucilages," Rheinhold Publishing Co., New York, N.Y., 1959.
4. D. M. W. Anderson and I. C. M. Dea, Recent advances in the chemistry of acacia gums, *J. Soc. Cosm. Chemists*, 22, 61-76 (1971).
5. J. Swarbrick, Coarse dispersions. In "Remington's Pharmaceutical Sciences," Chapter 22, 15th Ed., Mack Publishing Co., 1975.
6. "Toxicological Evaluation of Some Food Additives." Food and Agriculture Organization (WHO), FAO Nutrition Meeting Report Series No. 53A, 316-318, Rome, 1974.
7. Food Additives, *Federal Register*, 41, No. 236, 53608-53609, December 7, 1976.
8. The chemistry and rheology of water-soluble gums and colloids, *SCI Monograph No. 24*, Society of the Chemical Industry, London, 1966.

USA: E. Shefter*; J. Cooper*; J. W. Boenigk**

Alcohol

1. Nonproprietary Name

USP: Alcohol
BP: Ethanol (96%)

2. Functional Category

USP: Solvent
Others: Preservative

3. Synonyms

Ethanol; ethyl alcohol; grain alcohol; methyl carbinol

4. Chemical Names and CAS Registry Number

Ethanol
Ethyl alcohol [64-17-5]

5. Empirical Formula and Molecular Weight

Empirical Formula	Molecular Weight
C_2H_5OH	46.07

6. Structural Formula

C_2H_5OH

7. Commercial Availability

USA

Ashland Chemical Co.
Bage, Inc.
Clinton Corn Processing Co., Div. Nabisco Brands, Inc.
Eastman Chemical Products, Inc.
Mallinckrodt, Inc.
McKesson Chemical Co.
Publicker Industries, Inc.
Shell Chemical Co.
Stoney-Mueller, Inc.
Thompson-Hayward Chemical Co.
Union Carbide Corp.
U.S.I. Chemicals Co.

UK

Alcohols, Ltd.
BP Chemicals, Ltd.
Distillers Co., Ltd.
James Burroughs, Ltd.
Methylating Co., Ltd.
Unalco, Ltd.

8. Method of Manufacture

Whey, cellulose pulp and substances rich in starch or sucrose are subjected to controlled enzymatic hydrolysis fermentation to produce a fermented liquid which contains about 15% alcohol. The fermented liquid is fractionally distilled to produce alcohol which is 94.9-96.0% v/v (USP). Ethyl alcohol is also manufactured by converting ethylene into diethyl sulfate and then hydrolyzing the ester.

9. Description

A clear, colorless, mobile and volatile liquid with a slight, characteristic odor. It has a burning taste.

10. Pharmacopoeial Specifications

Test	USP	BP
Identification	+	+
Acidity or alkalinity	+	—
Nonvolatile residue	≤1 mg/40 ml	≤5 mg/100 ml
Specific gravity	0.812-0.816 at 15.56°C	0.8062-0.8087 at (20°/20°)
Aldehydes and other foreign organic substances	+	—
Amyl alcohol and nonvolatile carbonizable substances	+	—
Fusel oil constituents	+	—
Methanol	+	—
Water-insoluble substances	+	—
Aldehydes	—	≤10 ppm
Benzene	—	≤5 ppm
Clarity of solution	—	+
Reducing substances	—	+
Volatile impurities	—	+
Concentration range	94.9-96.0% v/v	96.0-96.6% v/v
Acetone and isopropyl alcohol	+	—

11. Typical Properties (All entries refer to dehydrated alcohol unless otherwise specified.)

Boiling point: 78.5°C (101.3 kN/m^2); 78.15°C (101.3 kN/m^2) minimum boiling point of azeotropic ethanol/water mixture.
Color: Hazen units—10 maximum (Pt-Co scale)
Flammability: Readily flammable, burning with a blue, smokeless flame.
Flash point (closed cup method): 12°C (100%); 14°C (96%)
Hygroscopicity: Absorbs water rapidly from the air.
Melting point: −117.3 to −114.1°C
Miscibility: (at 20°C): Water: Completely miscible, with rise of temperature and contraction in volume. Chloroform, acetone, ether and glycerin: Completely miscible.
Refractive index: 1.3611 (at 20°C)
Specific gravity: 0.7904-0.7935 (at 20°C); ≤0.7964 (at 15.56°C)
Surface tension: 22.75 mN/m (ethanol/vapor at 20°C)
Vapor density (relative): 1.59 (air = 1)
Vapor pressure: 5.3 kN/m^2 (at 19°C)
Viscosity: 1.20 mNs/m^2 (at 20°C)

12. Stability and Storage Conditions

Sterilized by autoclaving in sealed ampoules, or by filtration. Stable.
USP: Preserve in tight containers, remote from fire.
BP: Protect from moisture and store in a cool place.

13. Incompatibilities

In acidic solution, alcohol may react vigorously with oxidizing materials. Mixtures with alkali may darken in color due to the reaction with residual aldehydes in alcohol. Organic salts or acacia may be precipitated from aqueous solutions or dispersions.

14. Safety

Though alcohol has intoxicating properties, atmospheric concentrations sufficient to produce this effect are not generally reached in industry.

Threshold limit value (TLV) in workroom air in the United Kingdom is 1,000 ppm (of vapor by volume), or 1,900 mg/m^3. Exposure to concentrations of 5,000-10,000 ppm results in irritation of the eyes and mucous membranes of the upper respiratory tract. If continued for an hour, stupor and drowsiness may occur.

Preparations containing more than 50% ethanol may cause skin irritation when applied topically.

Systemically, alcohol is a CNS depressant. Sufficient doses can lead to nausea, vomiting, flushing, mental excitement or depression, drowsiness, impaired perception and incoordination. Severe overdosing can cause coma and death.

Oral LD_{50} (rat): 13.7 g/kg of body weight.

15. Handling Precautions

Fire/explosion hazard, dangerous when exposed to heat or flame.

Auto-ignition temperature: 390-430°C.

Explosive limits: 3.3-19.0% v/v in air.

Fixed storage tanks should be electrically grounded when ethanol is transferred.

Recommended extinguishers: Foam, CO_2, dry powder.

16. Regulatory Acceptance

USP XXI; BP 1980

17. Applications in Pharmaceutical Formulation or Technology

Use	Concentration (% v/v)
Preservative, bacteria and mold inhibitor	≥10
Disinfectant bactericide	60-90
Extracting solvent in galenical manufacture	Up to 85
Solvent in oral liquids	Variable
Solvent in film coating	Variable

18. Related Substances

Dehydrated alcohol, USP. Similar to alcohol USP, but contains not less than 99.5% v/v of C_2H_5OH.

Ethanol, BP. Contains 99.4-100.0% v/v C_2H_6O.

Diluted alcohol, NF. Content of C_2H_5OH is between 48.4% and 49.5% by volume.

The BP lists eight strengths of dilute ethanols, i.e., 90, 80, 70, 60, 50, 45, 25 and 20% v/v.

In the United States, the title "denatured alcohol" is used for ethyl alcohol which has been rendered unfit for human consumption by the addition of denaturing agents such as methanol and methyl isobutyl ketone.

Denatured ethanols for external use in the United Kingdom are industrial methylated spirit, BP, and surgical spirit, BPC 1973.

19. Comments

In the *European Pharmacopeia*, the term "ethanol" used without other indication means ethanol 99.5% v/v. The term "alcohol" without other indication means ethanol 95% v/v. Where other strengths are intended, the term "alcohol" is used, followed by the statement of the strength. The second edition of the *European Pharmacopeia* lists ethanol, alcohol and aldehyde-free alcohol only as reagents.

20. Specific References

1. V.D. Gupta, Effect of some formulation adjuvants on the stability of benzyl peroxide, *J. Pharm. Sci.*, 71(5):585, 587 (1982).
2. A.J. Spiegel and M.M. Noseworthy, Use of nonaqueous solvents in parenteral products, *J. Pharm. Sci.*, 52:917 (1963).
3. C.L. Lautenschlager and H. Schmidt, in *Sterilizations—Methoden Für Die Pharmazeutische Und Arztliche Praxis*, George Thieme, Verlag, 1954, p. 162.

USA: G.W. Radebaugh* Z. Chowhan**
UK: R.B. Forrester*

Alginic Acid

1. Nonproprietary Name

NF: Alginic acid

2. Functional Category

USP: Tablet binder, tablet disintegrant.
Others: Viscosity-increasing agent.

3. Synonyms

Polymannuronic acid; norgine

4. Chemical Name and CAS Registry Number

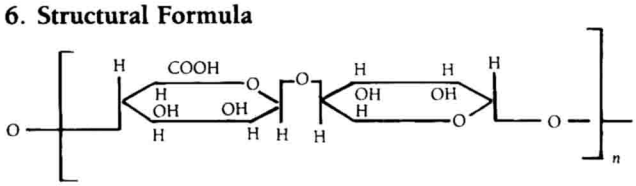
Alginic acid may be described chemically as a linear glycuronoglycan, consisting mainly of β-(1-4) linked D-mannuronic and L-guluronic acid units in the pyranose ring form.
Chemical Abstract Registry # [9005-32-7]

5. Empirical Formula / Molecular Weight

$(C_6H_8O_6)_n$

Approximately 240,000

6. Structural Formula



7. Commercial Availability

USA

Atomergic Chemetals Corp.
Colloides Naturels
Dormar Chemicals, Inc.
Edward Mendell Co., Inc.
Kelco Div. Merck & Co.
Pfaltz & Bauer, Inc.

UK

Alginate Industries, Ltd.
The British Ceca Co., Ltd.
Chemical Exchange (UK), Ltd.
Croxton & Garry, Ltd.

8. Method of Manufacture

Alginic acid is a hydrophilic colloid carbohydrate extracted with dilute alkali from various species of brown seaweed (Phaeophyceae).

9. Description

Alginic acid occurs as a white to yellowish-white, fibrous powder. It is practically odorless and tasteless.

10. Pharmacopeial Specifications

Test	NF	BP
Identification	+	+
Microbial limits	≤200/g tot. bact. NEG: *Salmonella species*, *Escherrchia coli*	– –
pH (3% dispersion)	1.5-3.5	–
Loss on drying (4 hrs. at 105°C)	≤15% (w/w)	18%
Ash	≤4%	–
Sulfated ash	–	≤7%
Lead	≤0.001%	≤10 ppm
Arsenic	≤3 ppm	≤3 ppm
Iron	–	≤300 ppm
Heavy metals	≤0.004%	–
Acid value	≥230	≥230

11. Typical Properties

Alginic acid is slightly soluble in water and insoluble in most organic solvents. It is soluble in alkaline solutions, resulting in viscous solutions. It is capable of absorbing 200-300 times its weight in water. Moisture content is approximately 7%.

Academy HPE Laboratory Project Data

Method	Lab #	Results
MC-8	18	7.01

Supplier: Mendell

12. Stability and Storage Conditions

Alginic acid, in warm storage areas, hydrolyzes very slowly, resulting in a decreasing molecular weight and lower solution viscosities. Store in a cool place in a well-closed container.

13. Incompatibilities

With the exception of magnesium, the alkaline earth metals and group III metals all form insoluble alginate salts.

14. Safety

Recorded toxicity:

Intraperitoneal in rat	LD_{50}	1600 mg/kg
Intravenous in mouse	LD_{50}	1000 mg/kg

15. Handling Precautions

—

16. Regulatory Acceptance

NF XVI; BPC 1973

17. Applications in Pharmaceutical Formulation or Technology

Use	Concentration
Tablet disintegrant	1-5%
Tablet binder	1-5%
Viscosity-increasing agent	—

18. Related Substances

—

19. Comments

Some loss of viscosity usually occurs in a solution prepared from sterilized alginic acid. The extent of this loss may be influenced by the presence of other added substances.
Alginic acid is best incorporated or blended into a tablet granulation by dry-mixing processes.

20. Specific References:

1. Literature issued by Kelco Company, San Diego, CA.
2. Literature issued by Edward Mendell Co., Carmel, NY.

USA: J. W. McGinity*; M. R. Harris*; R. Dusch*; W. A. Vadino**, J. Cooper**

Ascorbic Acid

1. Nonproprietary Names

USP: Ascorbic acid
BP/EP: Ascorbic acid

2. Functional Category

USP: Antioxidant

3. Synonyms

Vitamin C; L-ascorbic acid

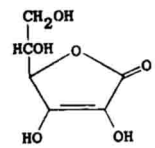
4. Chemical Names and CAS Registry Number

L-Ascorbic acid [50-81-7]
3-Oxo-L-gulofuranolactone (enol form)

5. Empirical Formula / Molecular Weight

$C_6H_8O_6$ — 176.1

6. Structural Formula



7. Commercial Availability

USA

American International Chemical, Inc.
Byron Chemical Co.
Dormar Chemicals, Inc.
E.M. Chemicals, Inc.
Fallek Chemical Co.
Gallard-Schlesinger Chemical Mfg. Corp.
Hoffmann-LaRoche, Inc.
ICC Industries, Inc.
Ingredients International, Inc.
Knoll Fine Chemicals, Div. Knoll Pharmaceutical Co.
Pardee Co., The
Pfizer, Inc.-Chemical Div.
Reisman Corp., H.
Salsbury Laboratories, Inc., Chemical Dept.
S.S.T. Corp.
Takeda-Fallek Sales, Inc.
Uhe Co., George
United States Biochemicals Corp.
Vitamins, Inc.

UK

Grindsted Products A/S
E. Merck
Pfizer, Ltd.
Roche Products, Ltd.
Takeda Chemical Industries, Ltd.

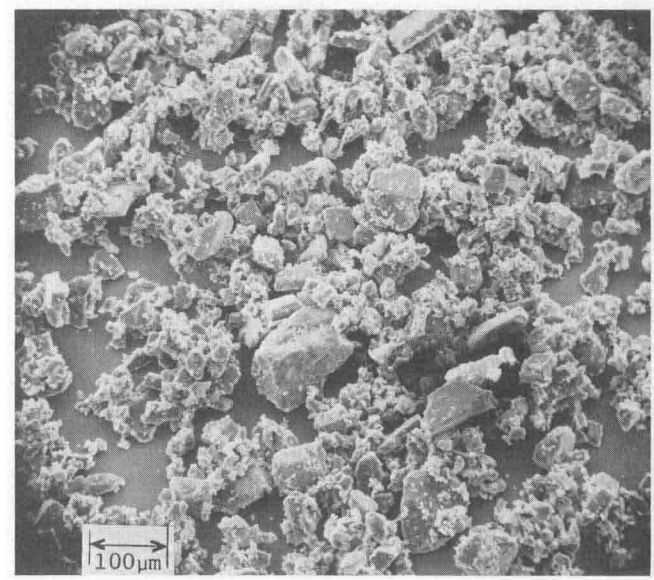
8. Method of Manufacture

Ascorbic acid is prepared synthetically or extracted from various vegetable sources in which it occurs naturally, such as rose hips, black currants, the juice of citrus fruits and the ripe fruit of *Capsicum annuum L.* A common synthetic procedure involves the conversion of D-glucose to D-sorbitol by hydrogenation. The resulting D-sorbitol is oxidized by *Acetobacter suboxydans* to L-sorbose. A carboxyl group is added at C_1 by air oxidation of the diacetone derivative of L-sorbose, and the resulting diacetone-2-keto-L-gulonic acid is converted to L-ascorbic acid when heated with hydrochloric acid.

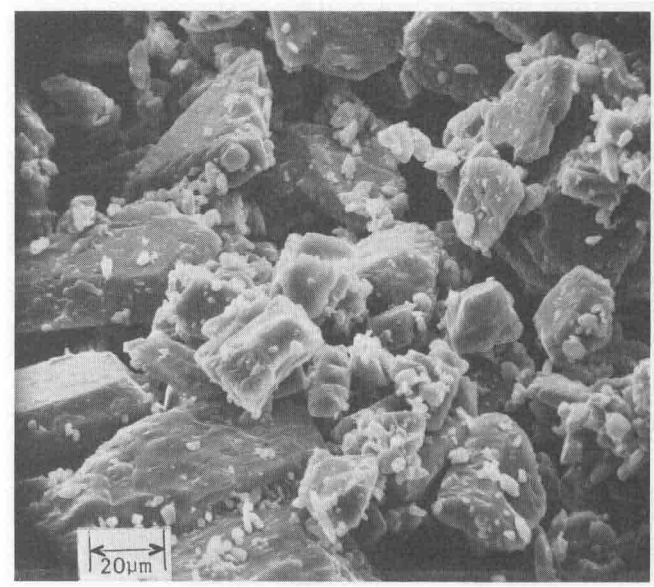
9. Description

White to light yellow, crystalline powder or colorless crystals with a sharp acidic taste and no odor. It is not hygroscopic. Upon exposure to light, it gradually darkens.

SEM: KY-8
Excipient: Ascorbic acid, USP fine powder
Manufacturer: Pfizer **Lot No.:** 9A-3/G92040-CO 146

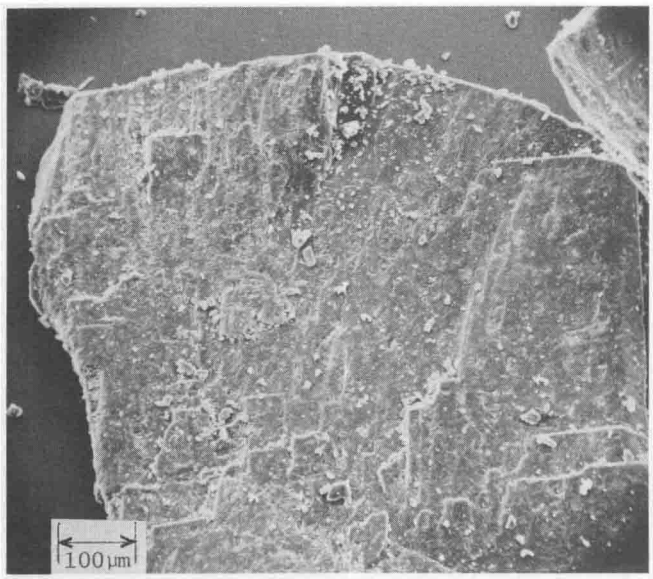


Magnification: 120× **Voltage:** 20 kV



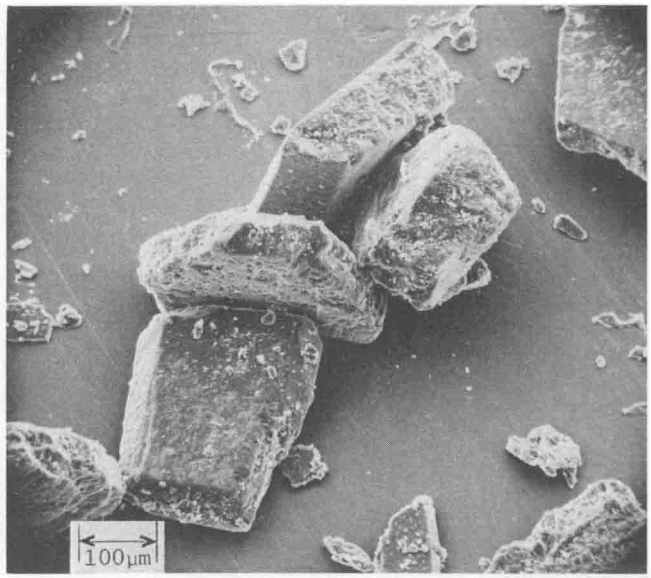
Magnification: 600× **Voltage:** 20 kV

SEM: KY-9
Excipient: Ascorbic acid USP granular
Manufacturer: Pfizer **Lot No.:** 9A-1/G01260-CO 140



Magnification: 120× **Voltage:** 20 kV

SEM: KY-10
Excipient: Ascorbic acid, USP fine granular
Manufacturer: Pfizer **Lot No.:** 9A-2/G01280-CO 148



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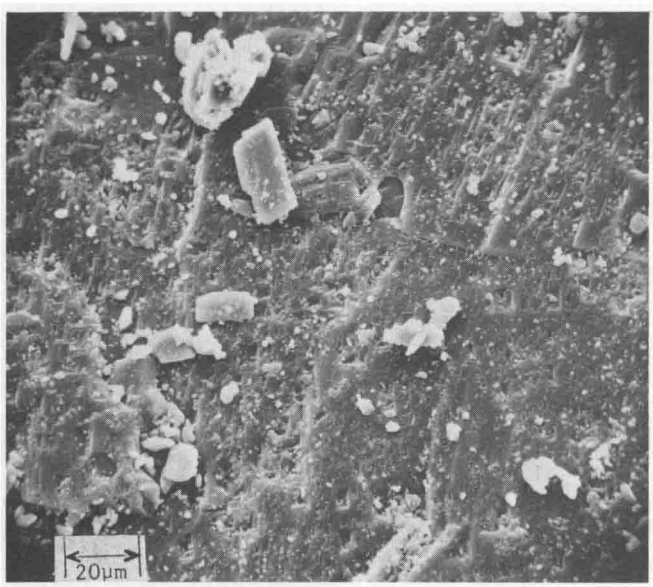
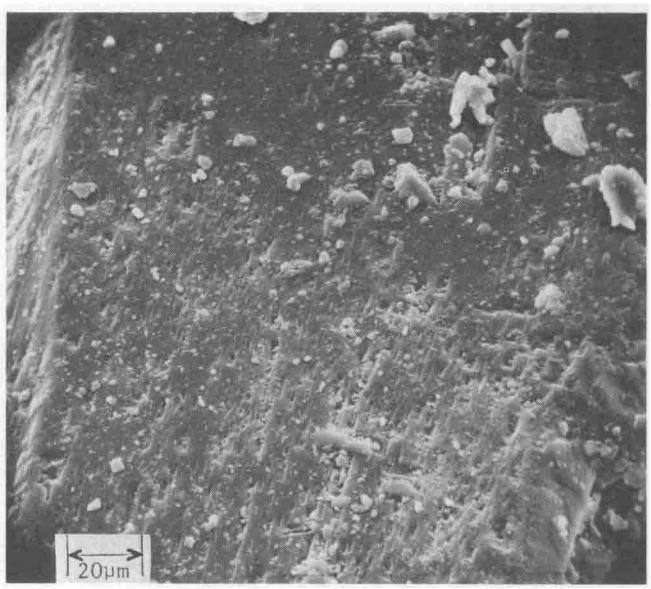


Magnification: 600× **Voltage:** 20 kV



Magnification: 600× **Voltage:** 20 kV