HANDBOOK OF PHARMACEUTICAL EXCIPIENTS

THIRD EDITION

EDITED BY

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Ethylcellulose

1. Nonproprietary Names

BP: Ethylcellulose
PhEur: Ethylcellulosum
USP: Ethylcellulose

2. Synonyms

Aquacoat; E462; Ethocel; *Surelease*.

3. Chemical Name and CAS Registry Number

Cellulose ethyl ether [9004-57-3]

4. Empirical Formula Molecular Weight

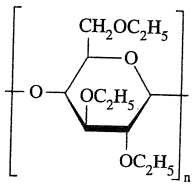
Ethylcellulose with complete ethoxyl substitution (DS = 3) is:

$$C_{12}H_{23}O_6(C_{12}H_{22}O_5)_nC_{12}H_{23}O_5$$

where n can vary to provide a wide variety of molecular weights. Ethylcellulose, an ethyl ether of cellulose, is a long-chain polymer of β-anhydroglucose units joined together by acetal linkages.

5. Structural Formula

The structures with complete ethoxyl substitution is given below.



6. Functional Category

Coating agent; flavoring fixative tablet binder; tablet filler; viscosity-increasing agent.

7. Applications in Pharmaceutical Formulation or Technology

Ethylcellulose is widely used in oral and topical pharmaceutical formulations, *see* Table I.

The main use of ethylcellulose in oral formulations is as a hydrophobic coating agent for tablets and granules.[1-7] Ethylcellulose coatings are used to modify the release of a drug,[7-9] to mask an unpleasant taste, or to improve the stability of a formulation, as is the case where granules are coated with ethylcellulose to inhibit oxidation. Modified-release tablet formulations may also be produced using ethylcellulose as a matrix former.[10-12]

Ethylcellulose, dissolved in an organic solvent, or solvent mixture, can be used on its own to produce water-insoluble films. Higher viscosity ethylcellulose grades tend to produce stronger and more durable films. Ethylcellulose films may be modified to alter their solubility,[13] by the addition of hydroxypropylmethylcellulose[14] or a plasticizer,[15-16] *see* Section 19. An aqueous polymer dispersion (or latex) of ethylcellulose such as *Aquacoat* (FMC Corp) or *Surelease* (Colorcon) may also be used to produce ethylcellulose films without the need for organic solvents. Drug release through ethylcellulose-coated dosage forms can be controlled by diffusion through the film coat. This can be a slow process unless a large surface area (e.g., pellets or granules vs. tablets) is utilized. In those instances, aqueous ethylcellulose dispersions tend therefore to be used to coat granules or pellets. Ethylcellulose-coated beads/granules have also demonstrated the ability to absorb pressure and hence protect the coating from fracture during compression.[17]

High viscosity grades of ethylcellulose are used in drug microencapsulation.[9,18-20]

Release of a drug from an ethylcellulose microcapsule is a function of the microcapsule wall thickness and surface area.

In tablet formulations, ethylcellulose may additionally be employed as a binder, the ethylcellulose being blended dry or wet-granulated with a solvent such as ethanol (95%). Ethylcellulose produces hard tablets with low friability; however, they may demonstrate poor dissolution.

Ethylcellulose has also been used as an agent for delivering therapeutic agents from oral (e.g., dental) appliances.[21]

In topical formulations, ethylcellulose is used as a thickening agent in creams, lotions, or gels, provided an appropriate solvent is used.

Ethylcellulose is additionally used in cosmetics and food products.

Table I. Uses and typical concentrations of ethylcellulose.

Use	Concentration (%)
Microencapsulation	10.0-20.0
Sustained-release tablet coating	3.0-20.0
Tablet coating	1.0-3.0
Tablet granulation	1.0-3.0

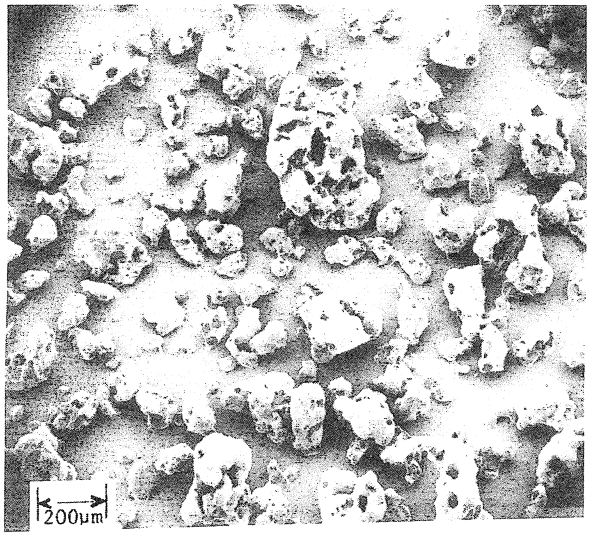
8. Description

Ethylcellulose is a tasteless, free-flowing, white to light tan colored powder.

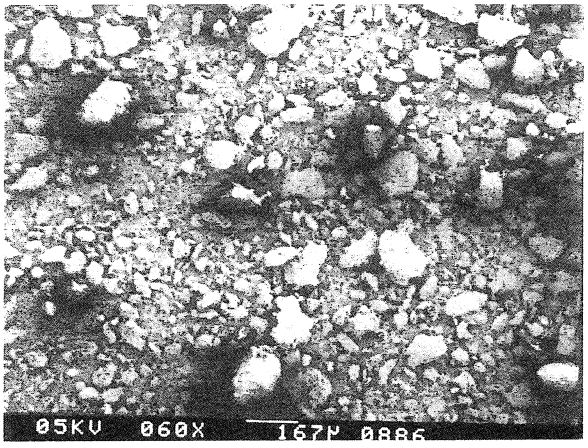
9. Pharmacopeial Specifications

Test	PhEur	USP
Identification	+	+
Characters	+	—
pH (2% w/w suspension)	5.0-7.5	—
Viscosity	+	+
Loss on drying	≤ 3.0%	≤ 3.0%
Residue on ignition	—	≤ 0.4%
Sulfated ash	≤ 0.5%	—
Lead	—	≤ 10 ppm
Heavy metals	≤ 20 ppm	≤ 20 µg/g
Acetaldehyde	≤ 100 ppm	—
Chlorides	≤ 0.1%	—
Organic volatile impurities	—	+
Assay (of ethoxyl groups)	44.0-51.0%	44.0-51.0%

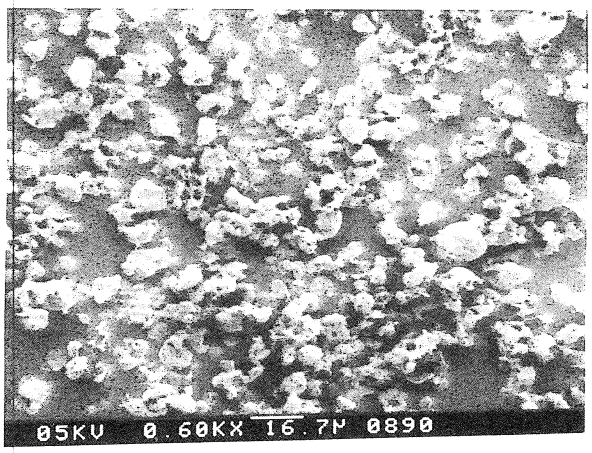
SEM: 1
Excipient: Ethylcellulose
Manufacturer: Hercules Ltd
Lot No: 57911
Magnfication: 60×
Voltage: 10 kV



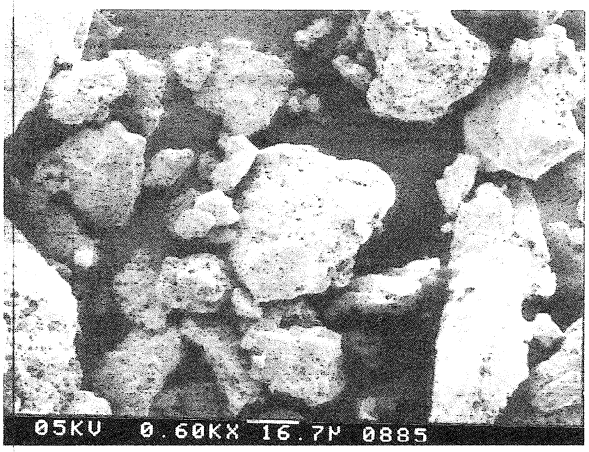
SEM: 2
Excipient: Ethylcellulose 10 cps fine powder
Manufacturer: Dow Chemical Co
Magnification: 60×
Voltage: 5 kV



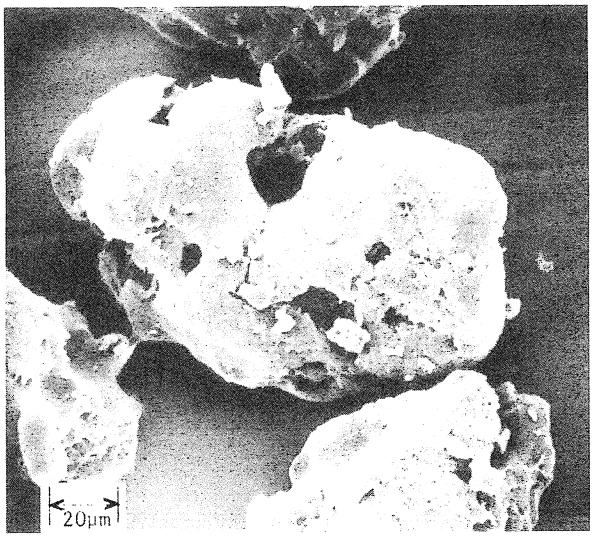
SEM: 3
Excipient: Ethylcellulose 10 cps fine powder
Manufacturer: Dow Chemical Co
Magnification: 600×
Voltage: 5 kV



SEM: 4
Excipient: Ethylcellulose 100 cps fine powder
Manufacturer: Dow Chemical Co
Magnification: 600×
Voltage: 5 kV



SEM: 5
Excipient: Ethylcellulose
Manufacturer: Hercules Ltd
Lot No: 57911
Magnfication: 600×
Voltage: 10 kV



SEM: 6
Excipient: Ethylcellulose (*Ethocel*)
Manufacturer: Dow Chemical Co
Lot No: 103051
Magnfication: 600×
Voltage: 10 kV

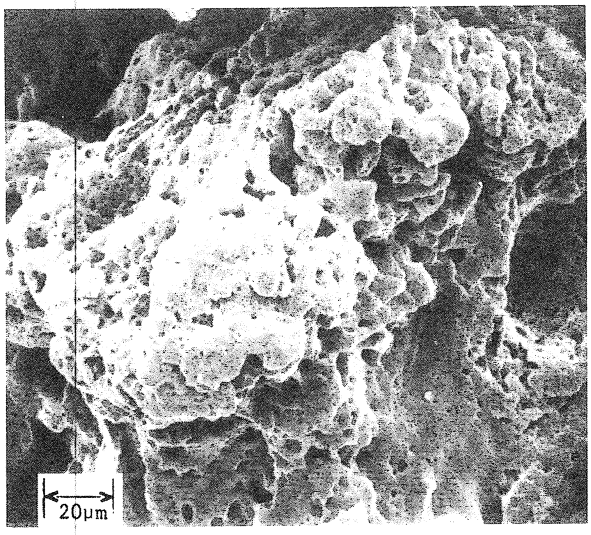


Table II. Moisture content of ethylcellulose as a function of equilibrium relative humidity.

Equilibrium relative humidity	Moisture %
11	0.3
23	0.6
33	0.9
43	0.9
52	1.3
64	2.2
75	2.7
83	3.3
93	5.0
100	—

Table III. Particle size analysis of ethylcellulose.

Ave. particle size (μm)	Cumulative % frequency oversized (wt.)	% Wt. retained
149	0	0.00
137	1.195	1.20
115	3.983	2.79
90	16.732	12.75
64	37.648	20.92
46	69.648	32.00

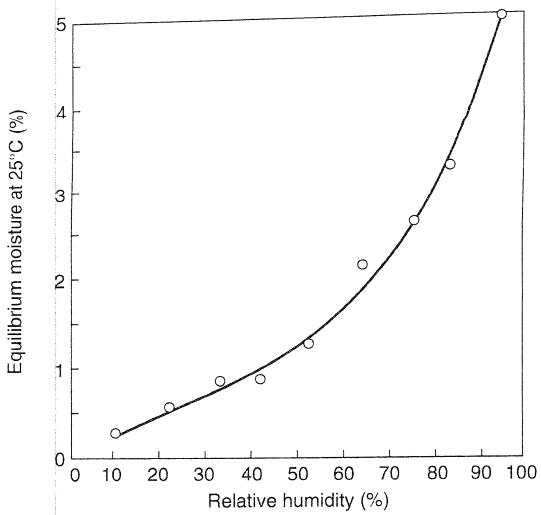


Fig. 1: Equilibrium moisture content of ethylcellulose.

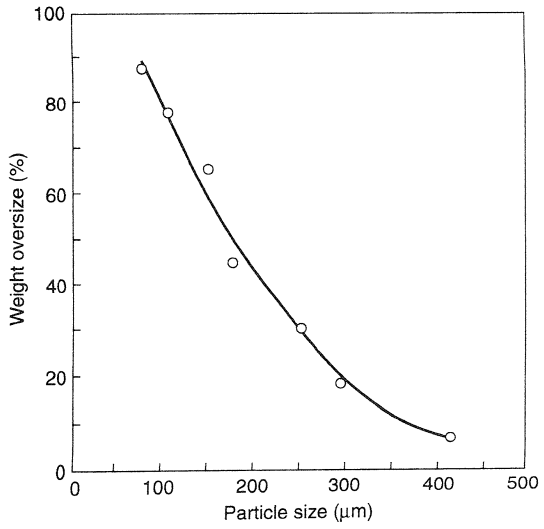


Fig. 2: Particle size distribution of ethylcellulose.

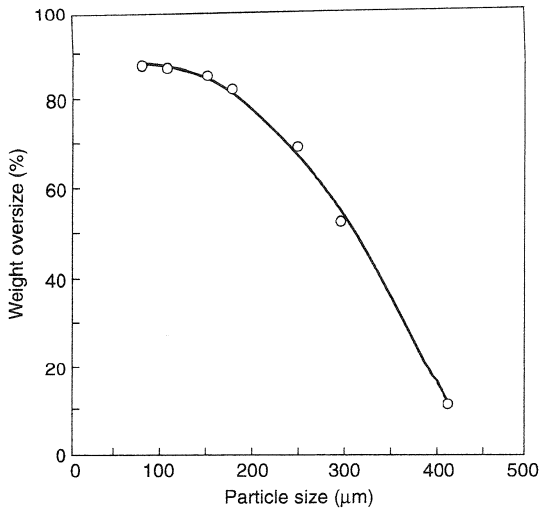


Fig. 3: Particle size distribution of ethylcellulose (*Ethocel*).

10. Typical Properties

Density (bulk): 0.4 g/cm^3

Glass transition temperature: 129-133°C[22]

Hygroscopicity: ethylcellulose absorbs very little water from humid air or during immersion, and that small amount evaporated readily.[23] The percent equilibrium moisture content as a function of relative humidity at 25°C for ethylcellulose, is shown in Table II. *See also* Fig. 1.[a]

Particle size distribution: *See* Table III and Figs. 2 and 3.[a]

Table IV. Summary of ethylcellulose grades, suppliers, viscosity, and particle size.

Grade	Supplier	Solution viscosity (mPa s)	Mean particle size (μm)
Ethocel Std 4 Premium	Dow Chemical	3-5.5	204
N-7	Aqualon	5.6-8	160
Ethocel Std 7FP Premium	Dow Chemical	6.0-8.0	9
Ethocel Std 7 Premium	Dow Chemical	6-8	210
N-10	Aqualon	8-11	225
Ethocel Std 10FP Premium	Dow Chemical	9.0-11.0	5
Ethocel Std 10P Premium			
N-14	Dow Chemical	9-11	212
Ethocel Std 20P Premium	Aqualon	12-16	—
N-22	Dow Chemical	18-22	243
Ethocel Std 45P Premium	Aqualon	18-24	—
N-50	Dow Chemical	41-49	305
N-100	Aqualon	40-52	—
Ethocel Std 100FP Premium	Aqualon	80-105	194
Ethocel Std 100P	Dow Chemical	90.0-110.0	40
	Dow Chemical	90-110	

Solubility: ethylcellulose is practically insoluble in glycerin, propylene glycol, and water. Ethylcellulose that contains less than 46.5% of ethoxyl groups is freely soluble in chloroform, methyl acetate, tetrahydrofuran, and in mixtures of aromatic hydrocarbons with ethanol (95%). Ethylcellulose that contains not less than 46.5% of ethoxyl groups is freely soluble in chloroform, ethanol (95%), ethyl acetate, methanol, and toluene.

Specific gravity: 1.12-1.15 g/cm^3

Viscosity: the viscosity of ethylcellulose is measured typically at 25°C using 5% ethylcellulose dissolved in a solvent blend of 80% toluene/20% ethanol (w/w). Various viscosity grades of ethylcellulose are commercially available (*see* Table IV). They may be used to produce 5% solutions in organic solvent blends with viscosities nominally ranging from 7 mPa s (7 cP) to 100 mPa s (100 cP). Specific ethylcellulose grades, or blends of different grades, may be used to obtain solutions of a desired viscosity. Solutions of higher viscosity tend to be composed of longer polymer chains and produce strong and durable films. The viscosity of an ethylcellulose solution increases with an increase in ethylcellulose concentration, e.g., the viscosity of a 5% w/v solution of *Ethocel Standard 4 Premium* is 4 mPa s (4 cP) and a 25% w/v solution of the same ethylcellulose grade is 850 mPa s (850 cP). Solutions with a lower viscosity may be obtained by incorporating a higher percentage (30-40%) of a low molecular weight aliphatic alcohol, such as ethanol, butanol, isopropanol, or *n*-butanol with toluene. The viscosity of such solutions depends almost entirely on the alcohol content and is independent of toluene.

In addition, nonpharmaceutical grades of ethylcellulose which differ in their ethoxyl content and degree of polymerization are also available.

[a] *Handbook of Pharmaceutical Excipients,* First Edition.

11. Stability and Storage Conditions

Ethylcellulose is a stable, slightly hygroscopic material. It is chemically resistant to alkalis, both dilute and concentrated, and to salt solutions. It is, however, more sensitive to acidic materials than cellulose esters.

Ethylcellulose is subject to oxidative degradation in the presence of sunlight or UV light at elevated temperatures. This may be prevented by the use of an antioxidant and chemical additives which absorb light in the 230-340 nm range.

Ethylcellulose should be stored at a temperature not exceeding 90°F (32°C) in a dry area away from all sources of heat. Do not store next to peroxides or other oxidizing agents.

12. Incompatibilities

Incompatible with paraffin wax and microcrystalline wax.

13. Method of Manufacture

Ethylcellulose is prepared by treating purified cellulose (sourced from chemical-grade cotton linters and wood pulp) with an alkaline solution followed by ethylation of the alkali cellulose with chloroethane:

$$RONa + C_2H_5Cl \rightarrow ROC_2H_5 + NaCl$$

where R represents the cellulose radical. The manner in which the ethyl group is added to cellulose can be described as the Degree of Substitution (DS) The DS designates the average number of hydroxyl positions on the anhydroglucose unit that have been reacted with ethyl chloride. Since each anhydroglucose unit of the cellulose molecule has three hydroxyl groups, the maximum value for DS is three.

14. Safety

Ethylcellulose is widely used in oral and topical pharmaceutical formulations. It is also used in food products. Ethylcellulose is not metabolized following oral consumption and is therefore a noncaloric substance. It is generally regarded as a nontoxic, nonallergenic, and nonirritating material. Ethylcellulose is not metabolized and therefore is not recommended for parenteral products; parenteral use may be harmful to the kidneys.

Since ethylcellulose is not considered to be a health hazard, the WHO has not specified an acceptable daily intake.[24]

15. Handling Precautions

It is important to prevent fine dust clouds of ethylcellulose from reaching potentially explosive levels in the air. Ethylcellulose is combustible. Ethylcellulose powder my be an irritant to the eyes and therefore eye protection should be worn.

16. Regulatory Status

Ethylcellulose is GRAS listed and is included in the FDA Inactive Ingredients Guide (oral capsules, suspensions and tablets, topical emulsions, and vaginal preparations).

17. Pharmacopeias

Eur, Int, and US.

18. Related Substances

Ethylcellulose is commercially available as a powder and as an aqueous colloidal dispersion or ethylcellulose aqueous dispersion. Other related water-insoluble cellulosic polymers include cellulose acetate butyrate, cellulose acetate, and cellulose nitrate. Methylcellulose is the closest chemically related substance.

19. Comments

Ethylcellulose is compatible with the following plasticizers: dibutyl phthalate; diethyl phthalate; dibutyl sebacate; triethyl citrate; tributyl citrate; acetylated monoglyceride; acetyl tributyl citrate; triacetin; dimethyl phthalate; benzyl benzoate; butyl and glycol esters of fatty acids; refined mineral oils; oleic acid; stearic acid; ethyl alcohol; stearyl alcohol; castor oil; corn oil; camphor.

20. Specific References

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22. Authors

TC Dahl.

Polymethacrylates

1. Nonproprietary Names

USP: Ammonio methacrylate copolymer
USP: Methacrylic acid copolymer

Note that two separate monographs applicable to polymethacrylates are contained in the USP; *see* Section 9.

2. Synonyms

Eastacryl 30D; *Eudragit*; *Kollicoat MAE 30 D*; *Kollicoat MAE 30 DP*; polymeric methacrylates.

3. Chemical Name and CAS Registry Number

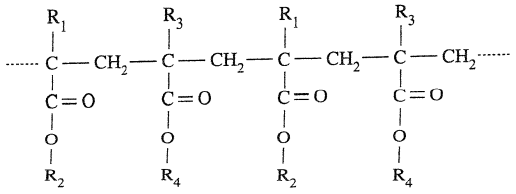
See Table I.

4. Empirical Formula and Molecular Weight

The USP describes methacrylic acid copolymer as a fully polymerized copolymer of methacrylic acid and an acrylic or methacrylic ester. Three types, Type A, Type B, and Type C, are defined in the monograph. They vary in their methacrylic acid content and solution viscosity. Type C may contain suitable surface-active agents. Two additional polymers, Type A (*Eudragit RL*) and Type B (*Eudragit RS*), also referred to as ammonio methacrylate copolymers, consisting of fully polymerized copolymers of acrylic and methacrylic acid esters with a low content of quaternary ammonium groups, are also described in the USP. *See* Section 9.

Typically, the molecular weight of the polymer is ≥100 000.

5. Structural Formula



For *Eudragit E*:

R_1, R_3 = CH_3
R_2 = $CH_2CH_2N(CH_3)_2$
R_4 = CH_3, C_4H_9

For *Eudragit L* and *S*:

R_1, R_3 = CH_3
R_2 = H
R_4 = CH_3

For *Eudragit RL* and *RS*:

R_1 = H, CH_3
R_2 = CH_3, C_2H_5
R_3 = CH_3
R_4 = $CH_2CH_2N(CH_3)_3^+Cl^-$

For *Eudragit NE 30 D*:

R_1, R_3 = H, CH_3
R_2, R_4 = CH_3, C_2H_5

For *Eudragit L 30 D-55* and *L 100-55*, *Eastacryl 30D*, *Kollicoat MAE 30 D and MAE 30 DP*

R_1, R_3 = H, CH_3
R_2 = H
R_4 = CH_3, C_2H_5

6. Functional Category

Film former; tablet binder; tablet diluent.

7. Applications in Pharmaceutical Formulation or Technology

Polymethacrylates are primarily used in oral capsule and tablet formulations as film-coating agents.[1-15] Depending on the type of polymer used, films of different solubility characteristics can be produced, *see* Table III.

Eudragit E is used as a plain or insulating film former; it is soluble in gastric fluid below pH 5. In contrast, *Eudragit L* and *S* types are used as enteric coating agents since they are resistant to gastric fluid. Different types are available which are soluble at different pH values, e.g., *Eudragit L 100* is soluble at > pH 6, *Eudragit S 100* is soluble at > pH 7.

Eudragit RL, *RS*, and *NE 30 D* are used to form water-insoluble film coats for sustained-release products. *Eudragit RL* films are more permeable than those of *Eudragit RS*, and by mixing the two types together films of varying permeability can be obtained.

Eudragit L 30 D-55 is used as an enteric coating film former for solid-dosage forms. The coating is resistant to gastric juice but readily dissolves at a pH above 5.5.

Eudragit L 100-55 is an alternative to *Eudragit L 30 D-55*. It is commercially available as a redispersible powder.

Eastacryl 30D, *Kollicoat MAE 30 D*, and *Kollicoat MAE 30 DP*, are aqueous dispersions of methacrylic acid/ethyl acrylate copolymers. They are also used as enteric coatings for solid-dosage forms.

Polymethacrylates are also used as binders in both aqueous and organic wet-granulation processes. Larger quantities (5-20%) of dry polymer are used to control the release of an active substance from a tablet matrix. Solid polymers may be used in direct-compression processes in quantities of 10-50%.

Polymethacrylate polymers may additionally be used to form the matrix layers of transdermal delivery systems and have also been used to prepare novel gel formulations for rectal administration.[16]

See also Section 19.

8. Description

Polymethacrylates are synthetic cationic and anionic polymers of dimethylaminoethylmethacrylates, methacrylic acid, and methacrylic acid esters in varying ratios. Several different types are commercially available and may be obtained as the dry powder, an aqueous dispersion, or as an organic solution. A (60:40) mixture of acetone and propan-2-ol is most commonly used as the organic solvent. *See* Tables I and II.

Table I: Chemical name and CAS Registry Number of polymethacrylates.

Chemical name	Trade name	Company name	CAS number
Poly(butyl methacrylate, (2-dimethyl aminoethyl) methacrylate, methyl methacrylate) 1:2:1	*Eudragit E 100*	Rohm GmbH	[24938-16-7]
	Eudragit E 12.5	Rohm GmbH	
Poly(ethyl acrylate, methyl methacrylate) 2:1	*Eudragit NE 30 D* (formerly *Eudragit 30 D*)	Rohm GmbH	[9010-88-2]
Poly(methacrylic acid, methyl methacrylate) 1:1	*Eudragit L 100*	Rohm GmbH	[25806-15-1]
	Eudragit L 12.5	Rohm GmbH	
	Eudragit L 12.5 P	Rohm GmbH	
Poly(methacrylic acid, ethyl acrylate) 1:1	*Eudragit L 30 D-55*	Rohm GmbH	[25212-88-8]
	Eudragit L 100-55	Rohm GmbH	
	Eastacryl 30D	Eastman Chemical	[25212-88-8]
	Kollicoat MAE 30 D	BASF Fine Chemicals	[25212-88-8]
	Kollicoat MAE 30 DP	BASF Fine Chemicals	
Poly(methacrylic acid, methyl methacrylate) 1:2	*Eudragit S 100*	Rohm GmbH	[25086-15-1]
	Eudragit S 12.5	Rohm GmbH	
	Eudragit S 12.5 P	Rohm GmbH	
Poly(ethyl acrylate, methyl methacrylate, trimethylammonioethy methacrylate chloride) 1:2:0.2	*Eudragit RL 100*	Rohm GmbH	[33434-24-1]
	Eudragit RL PO	Rohm GmbH	
	Eudragit RL 30 D	Rohm GmbH	
	Eudragit RL 12.5	Rohm GmbH	
Poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) 1:2:0.1	*Eudragit RS 100*	Rohm GmbH	[33434-24-1]
	Eudragit RS PO	Rohm GmbH	
	Eudragit RS 30 D	Rohm GmbH	
	Eudragit RS 12.5	Rohm GmbH	

Table II: Solubility of commercially available polymethacrylates in various solvents.

Type	Solvent						
	Acetone and alcohols[a]	Dichloromethane	Ethyl acetate	1N HCl	1N NaOH	Petroleum ether	Water
***Eudragit*, Röhm GmbH**							
Eudragit E 12.5	M	M	M	M	—	M	—
Eudragit E 100	S	S	S	—	—	I	I
Eudragit L 12.5 P	M	M	M	—	M	P	P
Eudragit L 12.5	M	M	M	—	M	P	P
Eudragit L 100-55	S	I	I	—	S	I	I
Eudragit L 100	S	I	I	—	S	I	I
Eudragit L 30 D-55[b]	M[c]	—	—	M[d]	—	M	
Eudragit S 12.5 P	M	M	M	—	M	P	P
Eudragit S 12.5	M	M	M	—	M	P	P
Eudragit S 100	S	I	I	—	S	I	I
Eudragit RL 12.5	M	M	M	—	—	P	M
Eudragit RL 100	S	S	S	—	—	I	I
Eudragit RL PO	S	S	S	—	I	I	I
Eudragit RL 30 D	M[e]	M	M	—	I	I	M
Eudragit RS 12.5	M	M	M	—	—	P	M
Eudragit RS 100	S	S	S	—	—	I	I
Eudragit RS PO	S	S	S	—	I	I	I
Eudragit RS 30 D	M[e]	M	M	—	I	I	M
***Eastacryl*, Eastman Chemical Company**							
Eastacryl 30D[b]	M[c]	—	—	—	M[d]	—	M
***Kollicoat*, BASF Fine Chemicals**							
Kollicoat MAE 30 D[b]	M[c]	—	—	—	M[d]	—	M
Kollicoat MAE 30 DP[b]	M[c]	—	—	—	M[d]	—	M

Where: S = soluble; M = miscible; I = insoluble or immiscible; P = precipitates.

[a] Alcohols including ethanol, methanol and propan-2-ol.

[b] Supplied as a milky-white colored aqueous dispersion.

[c] A 1:5 mixture forms a clear, viscous, solution.

[d] A 1:2 mixture forms a clear or slightly opalescent, viscous liquid.

[e] A 1 part of both *Eudragit RL 30 D* and *Eudragit RS 30 D* dissolve completely in 5 parts acetone, ethanol or propan-2-ol to form a clear or slightly turbid solution. However, when mixed in a ratio of 1:5 with methanol, *Eudragit RL 30 D* dissolves completely, whereas *Eudragit RS 30 D* only partially.

dragit E is cationic polymer based on dimethylaminoethyl thacrylate and other neutral methacrylic acid esters. It is uble in gastric fluid as well as in weakly acidic buffer utions (up to approximately pH 5). *Eudragit E* is available a 12.5% ready-to-use solution in propan-2-ol/acetone):40). It is light yellow in color with the characteristic odor the solvents. Solvent-free granules contain ≥98% dried ight content of *Eudragit E*.

dragit L and *S*, also referred to as methacylic acid copol- ıers in the USP monograph, are anionic copolymerization oducts of methacrylic acid and methyl methacrylate. The io of free carboxyl groups to the ester is approximately 1:1 *Eudragit L* and approximately 1:2 in *Eudragit S*. Both poly- ers are readily soluble in neutral to weakly alkaline condi- ons (pH 6-7) and form salts with alkalis, thus affording film ats which are resistant to gastric media but soluble in in- stinal fluid. They are available as a 12.5% solution in pro- an-2-ol without plasticizer (*Eudragit L 12.5* and *S 12.5*); and a 12.5% ready-to-use solution in propan-2-ol with 1.25% butyl phthalate as plasticizer (*Eudragit L 12.5 P* and *S 12.5*). Solutions are colorless, with the characteristic odor of the olvent. *Eudragit L-100* and *Eudragit S-100* are white free- owing powders with at least 95% of dry polymers.

udragit RL and *Eudragit RS*, also referred to as ammoni- methacrylate copolymers in the USP monograph, are copol- mers synthesized from acrylic acid and methacrylic acid sters with *Eudragit RL* (type A) having 10% of functional qua- ernary ammonium groups and *Eudragit RS* (type B) having 5% f functional quaternary ammonium groups. The ammonium groups are present as salts and give rise to pH-independent permeability of the polymers. Both polymers are water-insol- uble, and films prepared from *Eudragit RL* are freely perme- able to water, whereas, films prepared from *Eudragit RS* are only slightly permeable to water. They are available as 12.5% ready-to-use solutions in propan-2-ol/acetone (60:40). Solu- tions are colorless or slightly yellow in color, and may be clear or slightly turbid; they have an odor characteristic of the solvents. Solvent-free granules (*Eudragit RL 100* and *Eudragit RS 100*) contain ≥ 97% of the dried weight content of the polymer.

Eudragit RL PO and *Eudragit RS PO* are fine, white powders with a slight amine-like odor. They are characteristically the same poly- mers as *Eudragit RL* and *RS*. They contain ≥ 97% of dry polymer.

Eudragit RL 30 D and *Eudragit RS 30 D* are aqueous disper- sions of copolymers of acrylic acid and methacrylic acid es- ters with a low content of quaternary ammonium groups. The dispersions contain 30% polymer. The quaternary groups oc- cur as salts and are responsible for the permeability of films made from these polymers. Films prepared from *Eudragit RL 30 D* are readily permeable to water and to dissolved active substances, whereas films prepared from *Eudragit RS 30 D* are less permeable to water. Film coatings prepared from both polymers give pH-independent release of active substance. Plasticizers are usually added to improve film properties.

Eudragit NE 30 D is an aqueous dispersion of a neutral co- polymer consisting of polymethacrylic acid esters. The dis- persions are milky-white liquids of low viscosity and have a weak aromatic odor. Films prepared from the lacquer swell in water, to which they become permeable. Thus, films produced are in- soluble in water, but give pH-independent drug release.

Eudragit L 30 D-55, is an aqueous dispersion of an anionic copolymer based on methacrylic acid and ethyl acrylate. The copolymer corresponds to USP methacrylic acid copolymer, Type C. The ratio of free-carboxyl groups to ester groups is 1:1. Films prepared from the copolymers dissolve above pH 5.5 forming salts with alkalis, thus affording coatings which are insoluble in gastric media, but soluble in the small intestine.

Eastacryl 30D, Kollicoat MAE 30 D, and *Kollicoat MAE 30 DP* are also aqueous dispersions of the anionic copolymer based on methacrylic acid and ethyl acrylate. The copolymer also corresponds to USPNF methacrylic acid copolymer, Type C. The ratio of free-carboxyl groups to ester groups is 1:1. Films prepared from the copolymers dissolve above pH 5.5 forming salts with alkalis, thus affording coatings which are insoluble in gastric media, but soluble in the small intestine.

Eudragit L 100-55 (prepared by spray-drying *Eudragit L 30 D-55*) is a white, free-flowing powder which is redispersible in water to form a latex which has properties similar to *Eudragit L 30 D-55*.

9. Pharmacopeial Specifications

Specifications for methacrylic acid copolymers (*Eudragit L, S, L 30 D-55, Eastacryl 30D, Kollicoat MAE 30 D,* and *Kollicoat MAE 30 DP*).

Test	USP
Identification	+
Viscosity	
Type A	50-200 mPa s
Type B	50-200 mPa s
Type C	100-200 mPa s
Loss on drying	
Type A	≤ 5.0%
Type B	≤5.0%
Type C	≤ 5.0%
Residue on ignition	
Type A	≤0.1%
Type B	≤0.1%
Type C	≤ 0.4%
Arsenic	≤ 2 ppm
Heavy metals	≤ 0.002%
Monomers	≤ 0.3%
Assay of methacrylic acid units	
(dried basis)	
Type A	46.0-50.6%
Type B	27.6-30.7%
Type C	46.0-50.6%

Specifications for ammonio methacrylate copolymers (*Eudragit RL* and *RS*).

Test	USP
Identification	+
Viscosity	
Types A and B	≤ 15 mPa s
Loss on drying	
Types A and B	≤3.0%
Residue on ignition	
Types A and B	≤ 0.1%
Arsenic	≤ 2 ppm
Heavy metals	≤ 0.002%
Monomers	≤ 0.15%
Assay of ammonio methacrylate units (dried basis)	
Type A	8.85-11.96%
Type B	4.48-6.77%

Table III: Summary of properties and uses of commercially available polymethacrylates.

Type	Supply form	Polymer dry weight content	Recommended solvents or diluents	Solubility	Applications
***Eudragit*, Röhm GmbH**					
Eudragit E 12.5	Organic solution	12.5%	Acetone, alcohols to pH 5	Soluble in gastric fluid	Film coating
Eudragit E 100	Granules	98%	Acetone, alcohols	Soluble in gastric fluid to pH 5	Film coating
Eudragit L 12.5 P	Organic solution	12.5%	Acetone, alcohols	Soluble in intestinal fluid from pH 6	Enteric coatings
Eudragit L 12.5	Organic solution	12.5%	Acetone, alcohols	Soluble in intestinal fluid from pH 6	Enteric coatings
Eudragit L 100	Powder	95%	Acetone, alcohols	Soluble in intestinal fluid from pH 6	Enteric coatings
Eudragit L 100-55	Powder	95%	Acetone, alcohols	Soluble in intestinal fluid from pH 5.5	Enteric coatings
Eudragit L 30 D-55	Aqueous dispersion	30%	Water	Soluble in intestinal fluid from pH 5.5	Enteric coatings
Eudragit S 12.5 P	Organic solution	12.5%	Acetone, alcohols	Soluble in intestinal fluid from pH 7	Enteric coatings
Eudragit S 12.5	Organic solution	12.5%	Acetone, alcohols	Soluble in intestinal fluid from pH 7	Enteric coatings
Eudragit S 100	Powder	95%	Acetone, alcohols	Soluble in intestinal fluid from pH 7	Enteric coatings
Eudragit RL 12.5	Organic solution	12.5%	Acetone, alcohols	High permeability	Sustained release
Eudragit RL 100	Granules	97%	Acetone, alcohols	High permeability	Sustained release
Eudragit RL PO	Powder	97%	Acetone, alcohols	High permeability	Sustained release
Eudragit RL 30 D	Aqueous dispersion	30%	Water	High permeability	Sustained release
Eudragit RS 12.5	Organic solution	12.5%	Acetone, alcohols	Low permeability	Sustained release
Eudragit RS 100	Granules	97%	Acetone, alcohols	Low permeability	Sustained release
Eudragit RS PO	Powder	97%	Acetone, alcohols	Low permeability	Sustained release
Eudragit RS 30 D	Aqueous dispersion	30%	Water	Low permeability	Sustained release
Eudragit NE 30 D	Aqueous dispersion	30% or 40%	Water	Swellable, permeable	Sustained release, tablet matrix
***Eastacryl*, Eastman Chemical Company**					
Eastacryl 30 D	Aqueous dispersion	30%	Water	Soluble in intestinal fluid from pH 5.5	Enteric coatings
***Kollicoat*, BASF Fine Chemicals**					
Kollicoat 30 D	Aqueous dispersion	30%	Water	Soluble in intestinal fluid from pH 5.5	Enteric coatings
Kollicoat 30 DP	Aqueous dispersion	30%	Water	Soluble in intestinal fluid from pH 5.5	Enteric coatings

Note: Recommended plasticizers for the above polymers include dibutyl phthalate, polyethylene glycols, triethyl citrate, triacetin and 1,2-propylene glycol. The recommended concentration of the plasticizer is approximately 10 to 25% plasticizer (based on the dry polymer weight). A plasticizer is not necessary with *Eudragit E 12.5*, *Eudragit E 100* and *Eudragit NE 30 D*.

10. Typical Properties

Acid value:
300-330 for *Eudragit L 12.5*, *L 12.5 P*, *L 100*, *L 30 D-55*, *L 100-55*; *Eastacryl 30D*, *Kollicoat MAE 30 D*, and *Kollicoat MAE 30 DP*;
180-200 for *Eudragit S 12.5*, *S 12.5 P*, and *S 100*.

Alkali value:
162-198 for *Eudragit E 12.5* and E *100*;
23.9-32.3 for *Eudragit RL 12.5*, *RL 100*, and *RL PO*;
27.5-31.7 for *Eudragit RL 30 D*;
12.1-18.3 for *Eudragit RS 12.5*, *RS 100*, and *RS PO*;
16.5-22.3 for *Eudragit RS 30 D*.

Density (bulk): 0.390 g/cm^3

Density (tapped): 0.424 g/cm^3

Density (true):
0.811-0.821 g/cm^3 for *Eudragit E*;
0.83-0.85 g/cm^3 for *Eudragit L*, *S 12.5*, and *12.5 P*;
0.831-0.852 g/cm^3 for *Eudragit L*, *S 100*;
1.062-1.072 g/cm^3 for *Eudragit L 30 D-55*;
0.821-0.841 g/cm^3 for *Eudragit L 100-55*;
0.816-0.836 g/cm^3 for *Eudragit RL* and *RS 12.5*
0.816-0.836 g/cm^3 for *Eudragit RL* and *RS PO*;
1.047-1.057 g/cm^3 for *Eudragit RL* and *RS 30 D*;
1.037-1.047 g/cm^3 for *Eudragit NE 30D*;
1.062-1.072 g/cm^3 for *Eastacryl 30D*;
1.062-1.072 g/cm^3 for *Kollicoat MAE 30 D* and *Kollicoat MAE 30 DP*.

Refractive index:
n_D^{20} = 1.38-1.385 for *Eudragit E*;
n_D^{20} = 1.39-1.395 for *Eudragit L* and *S*;
n_D^{20} = 1.387-1.392 for *Eudragit L 100-55*;
n_D^{20} = 1.38-1.385 for *Eudragit RL* and *RS*.
Solubility: *see* Table II.
Viscosity (dynamic):
3-12 mPa s for *Eudragit E*;
≤ 50 mPa s for *Eudragit NE 30D*;
50-200 mPa s for *Eudragit L* and *S*;
≤ 15 mPa s for *Eudragit L 30 D-55*;
100-200 mPa s for *Eudragit L 100-55*;
≤ 15 mPa s for *Eudragit RL* and *RS*;
≤ 200 mPa s for *Eudragit RL* and *RS 30D*;
≤ 15 mPa s for *Kollicoat MAE 30 D* and *Kollicoat MAE 30 DP*;
145 mPa s for *Eastacryl 30D*.

11. Stability and Storage Conditions

Dry powder polymer forms are stable at temperatures less than 30°C. Above this temperature, powders tend to form clumps although this does not affect the quality of the substance and the clumps can be readily broken up. Dry powders are stable for at least 3 years if stored in a tightly closed container at less than 30°C.

Dispersions are sensitive to extreme temperatures and phase separation occurs below 0°C. Dispersions should therefore be stored at temperatures between 5-25°C and are stable for at least 18 months after shipping from the manufacturer's warehouse if stored in a tightly closed container at the above conditions.

12. Incompatibilities

Incompatibilities occur with certain polymethacrylate dispersions depending upon the ionic and physical properties of the polymer and solvent. For example, coagulation may be caused by soluble electrolytes, pH changes, some organic solvents, and extremes of temperature, *see* Table II. For example, dispersions of *Eudragit L 30 D*, *RL 30 D*, *L 100-55*, and *RS 30 D* are incompatible with magnesium stearate. *Eastacryl 30D*, *Kollicoat MAE 30 D*, and *Kollicoat MAE 30 DP* are also incompatible with magnesium stearate.

Interactions between polymethacrylates and some drugs can occur although solid polymethacrylates and organic solutions are generally more compatible than aqueous dispersions.

13. Method of Manufacture

Prepared by the polymerization of acrylic and methacrylic acids or their esters, e.g., butyl ester or dimethylaminoethyl ester.

14. Safety

Polymethacrylate copolymers are widely used as film-coating materials in oral pharmaceutical formulations. They are also used to in topical formulations and are generally regarded as nontoxic and nonirritant materials.

A daily intake of 2 mg/kg body-weight of *Eudragit* (equivalent to approximately 150 mg for an average adult) may be regarded as essentially safe in humans.

See also Section 15.

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Additional measures should be taken when handling organic solutions of polymethacrylates. Eye protection, gloves, and a dust mask or respirator are recommended. Polymethacrylates should be handled in well-ventilated environment and measures taken to prevent dust formation.

Acute and chronic adverse effects have been observed in workers handling the related substances methyl methacrylate and poly(methyl methacrylate) (PMMA).[17,18] In the UK, the occupational exposure limit for methyl methacrylate has been set at 410 mg/m^3 (100 ppm) long-term (8-hour TWA), and 510 mg/m^3 (125 ppm) short-term.[19]

See also Section 18.

16. Regulatory Status

Included in the FDA Inactive Ingredients Guide (oral capsules and tablets). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

US.

18. Related Substances

Methyl methacrylate: $C_5H_8O_2$
Molecular weight: 100.13
CAS number: [80-62-6]
Synonyms: methacrylic acid, methyl ester; methyl 2-methacrylate; methyl 2-methylpropenoate; MME.
Comments: methyl methacrylate forms the basis of acrylic bone cements used in orthopedic surgery.

Poly(methyl methacrylate): $(C_5H_8O_2)_n$
Synonyms: methyl methacrylate polymer; PMMA.
Comments: poly(methyl methacrylate) has been used as a material for intra-ocular lenses, for denture bases, and as a cement for dental prostheses.

19. Comments

A number of different polymethacrylates are commercially available which have different applications and properties, *see* Table III.

For spray coating, polymer solutions and dispersions should be diluted with suitable solvents. Some products need the addition of a plasticizer such as: dibutyl sebacate; dibutyl phthalate; glyceryl triacetate and polyethylene glycol. Different types of plasticizer may be mixed to optimize the polymer properties for special requirements.

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22. Authors

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