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Basic Concepts Of Cellulose Polymers- A Comprehensive Review

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Abstract

Man's pursuance for new and improved materials has been expanding with time and it can be said that it is unending. Though introduced very late in the chain of materials, polymers occupy a major place and pivotal position in our materials map today. Unfolding of the science of polymers and polymer – based materials had evoked lot of interest and made them as a class of materials for their potential use in the field of pharmaceuticals and industry based products. In recent years, an awareness and understanding of these polymers has increased based upon the following factors.

- As pharmaceutically active ingredients continue to become more ''potent'' the effective controlled delivery of doses have become intriguing. As a result, polymers now often constitute the major portion of many pharmaceutical dosage forms and as such can have profound impact on the reproducibility of drug release and overall performance of the dosage forms.
- The technical complexities associated with drug development have increased in controlled delivery due to challenges such as complex drug actives, and in cases of biotech products, stabilization of the active ingredient. The multidisciplinary understanding of polymers is thus required including technical, safety, quality, and regulatory aspects, which, prior to this effort, has not been available in a single resource.
- It also proposes new and innovative ways for regulatory review of polymers, which, if adopted, should promote innovation. To assist the exploitation of novel drug delivery systems the need for polymers continues to increase.

This review serves as a comprehensive source to improve understanding of cellulose derivative polymers and create new avenues in development of a delivery system. In addition, this review presents in-depth information on various aspects of polymer chemistry, nomenclature, various polymer grades, physical characteristics of polymers, solubility, and the utility of polymers for various drug delivery systems.

Key words

Cellulose Polymers, Premium Product Grades, Viscosities, Solubility.

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Introduction

Cellulose is the most copious naturally occurring "biopolymer". The main constituent of various natural fibers such as cotton and higher plants is cellulose. It consists of long chains of anhydro-D-glucopyranose units (AGU) with each cellulose molecule having three hydroxyl groups per AGU, except at the terminal ends. Cellulose is insoluble in water and most common solvents; the poor solubility is accredited primarily to the strong intramolecular and intermolecular hydrogen bonding between the individual chains. Regardless of its poor solubility characteristics, cellulose is used in a wide range of applications including composites, netting, upholstery, coatings, packing, paper, etc. Cellulose is chemically modified to improve process ability and to produce cellulose derivatives (cellulosics) which can be tailored for specific industrial applications [1-5]. Cellulosics are in general strong, reproducible, recyclable and biocompatible, being used in various biomedical applications such as blood purification membranes and the like. Thus, through derivatization, cellulosics have opened a window of opportunity and have broadened their use.

Cellulose derivatives are a branch of semi-synthetic polymers used in controlled drug delivery. In this review, we summarize all the critical properties of cellulose ethers that can be utilized for fulfilling the need of controlling the release of active ingredient from a drug delivery system.

Chemically modified derivatives of cellulose:

Cellulose (Fig 1) being water insoluble, etherification and esterification at hydroxyl groups bring about drastic changes in its original properties making its derivatives soluble in organic and aqueous solvents [6]. The hydroxyl groups (-OH) of cellulose can be partially or fully reacted with various reagents to afford derivatives with useful properties like mainly cellulose esters and cellulose ethers (-OR).

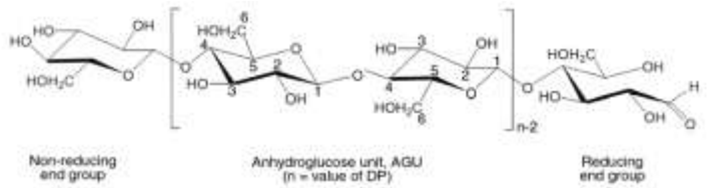


Figure 1: Molecular structure of cellulose

Etherification: Cellulose ethers can be prepared by treating alkali cellulose with a number of various reagents including alkyl or aryl halides (or sulfates), alkene oxides, and unsaturated compounds activated by electron-attracting groups (Eq 1).

$$\underset{\text{alcohol}}{ROH} + \underset{\text{alkylchloride}}{R'Cl} \longrightarrow \underset{\text{ether}}{ROR'} + \underset{\text{hydrogen chloride}}{HCl}$$

Equation 1: Etherification of cellulose. R'= organic radical (CH_3-, C_2H_5–, etc)

Table 1: Ether derivatives [6,7]

Cellulose ethers	Reagent	Example	Reagent
Alkyl	Halogeno alkanes	Methylcellulose	Chloromethane
		Ethylcellulose	Chloroethane
		Ethyl methyl cellulose	Chloromethane and chloroethane
Hydroxy alkyl	Epoxides	Hydroxyethyl cellulose	Ethylene oxide
		Hydroxypropyl cellulose (HPC)	Propylene oxide
		Hydroxyethyl methyl cellulose	Chloromethane and ethylene oxide
		Hydroxypropyl methyl cellulose (HPMC)	Chloromethane and propylene oxide
		Ethyl hydroxyethyl cellulose	Chloroethane and ethylene oxide
Carboxy alkyl	Halogenated carboxylic acids	Carboxymethyl cellulose (CMC)	Chloroacetic acid

The sodium carboxymethyl cellulose can be cross-linked to give the croscarmellose sodium (E468) for use as a disintegrant in pharmaceutical formulations.

Esterification: The esterification can be considered as a typical equilibrium reaction in which an alcohol and acid react to form ester and water. Cellulose is esterified with certain acids such as acetic acid, nitric acid, sulfuric acid and phosphoric acid.

Table 2: Ester derivatives [6]

Cellulose ester	Reagent	Example	Reagent
Organic esters	Organic acids	Cellulose acetate	Acetic acid and acetic anhydride
		Cellulose triacetate	Acetic acid and acetic anhydride
		Cellulose propionate	Propanoic acid
		Cellulose acetate propionate	Acetic acid and propanoic acid
		Cellulose acetate butyrate	Acetic acid and butyric acid
Inorganic esters	Inorganic acids	Nitrocellulose (cellulose nitrate)	Nitric acid or another powerful nitrating agent
		Cellulose sulfate	Sulfuric acid or another powerful sulfuring agent

Cellulose acetate phthalate is obtained by partial substitution of cellulose acetate (CA) with phthalic anhydride in the presence of an organic solvent and a basic catalyst.

METHOD HOW THE INFORMATION WAS GATHERED/ CRITERIA FOR THE SELECTION OF ARTICLES

- Information was gathered from product brochures of chemical companies (Dow, Hercules, Aqualon, WeKcelo) which are synthesizing these polymers.
- Physical description of the materials was obtained from Material safety data sheet (MSDS) of these particular polymers.
- Other information was also considered from monographs of the different pharmacopeias.
- Some basic concepts about the cellulosic polymers were obtained from articles published in various journals.

PROPERTIES OF CELLULOSE DERIVATIVE POLYMERS

Cellulose ethers: The factors associated with polymers, such as molecular weight, viscosity, concentration, degree of substitution and particle sizes have a significant influence on drug release. Hence, it is necessary to have thorough knowledge of the polymer properties to choose the suitable polymer to control the release from a particular dosage form. Among the known polymers, cellulose ethers are materials of choice for controlled drug release which are discussed in detail in this review.

Table 3: A Versatile Range of Polymer Properties [8]

PROPERTIES	METHYL CELLULOSE	ETHYL CELLULOSE	HPMC &HPC	HEC	CMC	CELLULOSE ACETATE	NITRO CELLULOSE
Water soluble	●		●	●	●		
Organo soluble	●	●	●			●	●
Gel forming	●		●	●	●		
Film forming	●	●	●	●	●	●	●
Mucoadhesive	●		●	●	●		
High swelling	●		●	●	●		
Hydrophilic	●		●	●	●		
Hydrophobic		●				●	
Viscosifying	●	●	●	●	●	●	●
Thermoplastic		●				●	●
Drug solubilizer	●		●	●	●		

A. Methyl cellulose and hypromellose:

Premium methyl cellulose and hypromellose products are a broad range of water soluble cellulose ethers. They enable pharmaceutical developers to create reliable formulas for tablet coating, granulation, controlled release, extrusion, molding and for controlled viscosity of liquid formulations.

Chemistry of methyl cellulose ethers:

These products are available in two basic types: methyl cellulose (Fig 2) and HPMC (Fig 3). Methyl cellulose is made using only methyl chloride. These are methocel A brand products. For HPMC products (methocel E, F, J and K brand products) propylene oxide is used in addition to methyl chloride to obtain hydroxy propyl substitution on anhydroglucose units. Both types have the polymeric backbone of cellulose but possess different ratios of hydroxypropyl to methoxyl substitution. These ratios largely determine the properties of different product grades and in particular influence hydrophilicity, gelling behavior, rheology, surface activity and film forming [9].

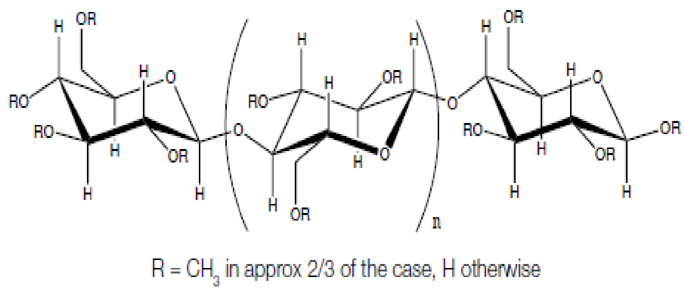


Figure 2: Chemical structure of methyl cellulose

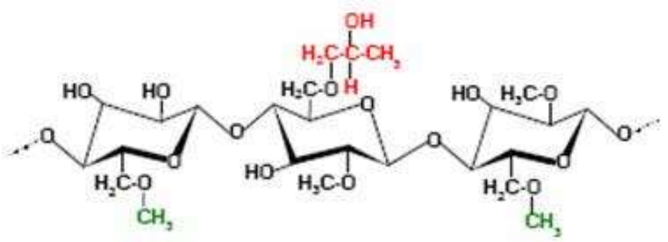


Figure 3: Chemical Structure of Hydroxypropyl Methylcellulose

Nomenclature:

An example [10]-

HPMC E 15 premium LV

- LV → Low viscosity
- premium → For pharmaceutical use
- 15 → Viscosity (15 mPa.s for a 2% solution in water at 20°C)
- E → Chemistry type: E and K are hypromellose; A is methylcellulose

The initial letter in the product name identifies the type of cellulose ether, as follows [11]:

- "A" : methyl cellulose products
- "E", "F", "J" and "K": hydroxyl propyl methylcellulose products

The number that follows the initial letter identifies the viscosity grade in milli-pascal seconds (**Note: milli pascals second is equal to centipoises, cP**) for the product measured at 2% in water at 20°C. A "C" or an "M" following this number indicates that it is multiplied by the following number:

- "C": 100 times
- "M": 1,000 times

Finally, here are some commonly used suffixes that identify special products:

- LV, low viscosity
- S, surface treated (cold water dispersible) products
- G, granular products
- CR, controlled release grade
- FG, food grade
- P, premium grade
- PCG or AMC, personal care grade
- Developmental grades are denoted by letter "X" plus a second letter (usually U or Y) plus a five digit code

The three digit suffix uniquely identifies particular

products offered which differ in substitution ratio and viscosity. Here are some other examples:
METHOCEL A 4 CP- methylcellulose product with viscosity of 400 mPa.s, Premium grade
METHOCEL E 4 M PAMC- hydroxypropyl methyl cellulose product with viscosity of 4,000 mPa.s, personal care grade that also meets premium grade requirements

Table 4: Methyl cellulose product grades [12,13]

Product	Chemical type	Available viscosities, cps	Methoxy %	Hydroxypropyl %	Avg particle size (µm)
Methocel A premium	Methyl cellulose USP	15, 400, 1,500, 4,000	27.5-31.5	0	85.6
Methocel E premium	Hypromellose 2910	3, 5, 6, 15, 50, 400, 10,000	28.8-30	7-12	72.2
Methocel F premium	Hypromellose 2906	50, 4,000	27-30	4-7.5	65
Methocel J premium			16.5-20	23-32	88.4
Methocel K premium	Hypromellose 2208	3, 100, 4,000, 15,000 1,00,000	19-25	4-12	64.7
Methocel 310 series			25	25	100-500

- METHOCEL E Premium products are also available in faster hydrating CR (controlled release) grades for 50, 4,000, and 100,000 cps products
- METHOCEL K Premium products are also available in faster hydrating CR (controlled release) grades for 100, 4,000, 15,000 and 100,000 cps products
- Viscosities for METHOCEL Premium products are for 2% solutions in H_2O at 20°C

Table 5: Description of methyl cellulose premium products (USP specifications) [14]

Properties	Description
Physical appearance	White to slightly off-white, essentially odorless and tasteless powder
Particle size	100%, No. 30 screen; 99%, No. 40 screen
Apparent density, g/cc	0.25-0.70
pH (2% w/w solution)	5.0-8.0
Melting point	Glass transition temperature is 170-180°C
Max. moisture content, %	5.0

Solubility:

- Practically insoluble in acetone, methanol, chloroform, ethanol (95%), ether, saturated salt solutions, toluene and hot water.
- In cold water, methylcellulose swells and disperses slowly to form a clear to opalescent, viscous, colloidal dispersion.
- Soluble in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane, and mixtures of water and alcohol.
- Certain grades of hypromellose are soluble in aqueous acetone solutions, mixtures of dichloromethane and propan-2-ol, and other organic solvents.
- Soluble in glacial acetic acid and in a mixture of equal volumes of ethanol and chloroform.
- Some grades are swellable in ethanol.

In general, binary solvent systems functions more effectively with methyl cellulose products than single solvents. Where alcohols comprise part of binary solvent, solubility improves as the molecular weight of alcohol decreases.
Typical nonaqueous solvents used with methyl cellulose ethers [9]:

- Furfuryl alcohol
- Dimethyl formamide
- Dimethyl sulphoxide
- Formic acid
- Glacial acetic acid
- Mixtures of methylene chloride and ethyl, methyl, or isopropyl alcohols
- Mixtures of chloroform and methanol or ethanol
- N-methyl pyrrolidone

Solvent solubility at elevated temperatures [9]: Methocel E and Methocel J cellulose ether products possess structures that provide unusual solubility properties. They are soluble in certain nonaqueous media at elevated temperatures.

Table 6: Examples of suitable "hot solvents"

Solvent	Boiling point °C	Solubility point °C	Degree of solubility
Glycols			
Ethylene glycol	197.3	158	Completely soluble
Diethylene glycol	244.8	135	Completely soluble
Propylene glycol	188.2	140	Completely soluble
1,3-propanediol	214	120	Completely soluble
Glycerine	290	260	Partially soluble
Esters			
Ethyl glycolate	160	110	Completely soluble
Glyceryl monoacetate	127	100	Completely soluble
Glyceryl diacetate	123-133	100	Completely soluble
Amines			
Monoethanolamine	170-172	120	Completely soluble
Diethanolamine	268-269	180	Completely soluble

Methocel 310 series products: They are granular, high viscosity materials. Their carefully balanced level of substitution renders them soluble in both water and certain organic solvents or blends of solvents.

B. Ethyl cellulose:

Ethyl cellulose is a family of organo-soluble thermoplastics that have been widely used in pharmaceuticals. Ethyl cellulose products are among only a very small number of water insoluble excipient polymers that are approved and accepted globally for pharmaceutical applications [15]. By themselves, they offer an attractive range of physical properties and they can be blended with other materials to achieve intermediate characteristics.

Chemistry of ethyl cellulose ethers:
Like cellulose, the backbone of the molecule of ethyl cellulose (Fig 4) is based on repeating anhydroglucose units. Specific properties of the various ethyl cellulose polymers are determined by the number of anhydroglucose units in the polymer chain and the degree of ethoxyl substitution.

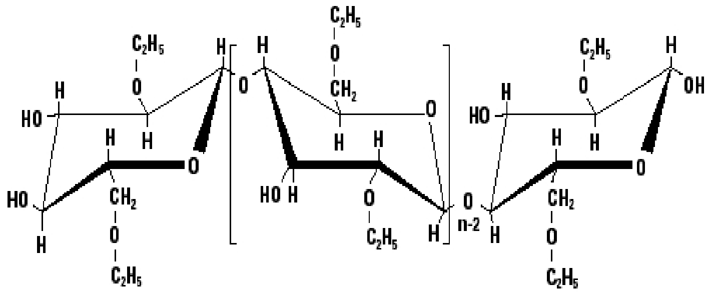
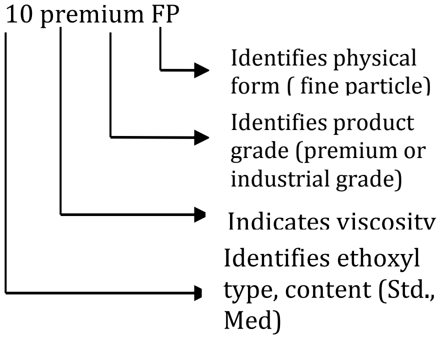


Figure 4: Chemical structure of ethyl cellulose

Nomenclature:
An Example-
ETHYL CELLULOSE Std. 10 premium FP



The letters following trade mark name (i.e., STD, Med) identify the ethoxyl type and ethoxyl content (the chemical designation). "Standard" polymers have an ethoxyl content of 48.0 to 49.5%; and "medium" polymers have an ethoxyl content of 45.0 to 47.0%. Medium polymers are supplied on a very restricted, made-to-order basis only.
The number that follows the chemistry designation identifies the viscosity of that product in milli Pascals second. Viscosity of a 5% solution is measured at 25°C. For medium products solvent is 60% toulene and 40% ethanol. For all other ethyl cellulose products, solvent is 80% toluene and 20% ethanol.
For example, ethyl cellulose STD. 20 premium polymer describes a product with [16]:

- Standard ethoxyl content (48.0- 49.5%).
- Nominal viscosity of 20 mPa.s for a 5% solution (in 80% toluene and 20% ethanol) measured at 25°C.
- Intended use in pharmaceuticals or other regulated applications.

Table 7: Ethyl cellulose product grades [15, 16]

Product viscosity designation	Viscosity range mPa.s (cP)	Ethoxyl content, %		Mean particle size (µm)
		Std	Med	
ETHOCEL Std 4 premium	3-5.5	48.0-49.5%		
ETHOCEL Std 7 premium	6-8	48.0-49.5%		310.0
ETHOCEL Std 7FP premium	6-8	48.0-49.5%		5.0-15.0
ETHOCEL Std 10 premium	9-11	48.0-49.5%		375.0
ETHOCEL Std 10FP premium	9-11	48.0-49.5%		3.0-15.0
ETHOCEL Std 14 premium[a]	12.6-15.4	48.0-49.5%		
ETHOCEL Std 10 premium	18-22	48.0-49.5%		
ETHOCEL Std 45 premium	41-49	48.0-49.5%		
ETHOCEL Med 50 premium[a]	45-55		45.0-46.5%	
ETHOCEL Med 70 premium[a]	63-77		45.0-46.5%	
ETHOCEL Std 100 premium[a]	90-110	48.0-49.5%	45.0-46.5%	465.0
ETHOCEL Std 100FP premium	90-110			30-60
ETHOCEL Std 200 premium	180-220	48.0-49.5%		
ETHOCEL Std 300 premium	270-330	48.0-49.5%		

(a) Supplied on a restricted, made-to-order basis only.

Fine particle size products were designed specifically for pharmaceutical formulations when the ethocel is used in an unsolubilized form such as in direct compression controlled release tablets, granulation and/or agglomeration. In these applications, the particle size distribution influences the release rate and tablet compressibility.

Table 8: Description of ethyl cellulose premium products (USP specifications) [17]

Properties	Description
Physical appearance	White , essentially odorless and tasteless powder
Density, g/cc (ethocel STD 4,7,10,20,45,100)	0.4
Density, g/cc (ethocel STD 200& 300)	0.3
pH	Neutral to litmus
Melting point	165-173°C Glass transition temperature 129–133°C
Max. moisture content, %	5.0
Specific gravity, g/cc	1.12-1.15

Solubility:

- Ethyl cellulose is practically insoluble in glycerin, propylene glycol, and water, but soluble in varying proportions in certain organic solvents, depending upon the ethoxyl content.
- Ethylcellulose that contains less than 46.5% of ethoxyl groups is freely soluble in chloroform, methyl acetate, and tetrahydrofuran, and in mixtures of aromatic hydrocarbons with ethanol (95%).
- Ethylcellulose that contain not less than 46.5% of ethoxyl groups is freely soluble in chloroform, ethanol (95%), ethyl acetate, methanol and toluene [18-24].

Table 9: Solubility of ethyl cellulose polymers in a number of common single solvents [16]

Solvent		Solubility[a] of ethyl ceullulose polymers	
A. HYDROCARBONS			
Type	**Name of solvent**	**Standard ethoxyl**	**Medium ethoxyl**
Aromatic hydrocarbons	Toluene, xylene	Sol clear	Gels
	Ethyl benzene	Sol clear	Sol gels
	Isopropyl benzene	Sol clear	Swells
	Diethyl benzene, diphenyl ethane	Sol gels	Swells
Cyclo aliphatic hydrocarbons	Cyclo hexane, methyl cyclohexane	Swells	Insol
	Cyclo hexene	Sol clear	Sol clear
Chlorinated aliphatic hydrocarbons	Chloroform, ethylene dichloride, trichloro ethylene, propylene dichloride, trichloro ethane, tetrachloro ethane, methylene chloride	Sol clear	Sol clear
	Carbon tetra chloride	Sol clear	Gels
	Perchloroethylene	Sol hazy	Swells
Chlorinated aromatic hydrocarbons	Monochloro benzene, o-dichloro benzene	Sol clear	Sol hazy
	Trichloro benzene	Sol clear	Swells
B. ALCOHOLS AND ETHERS			
Monohydric aliphatic alcohols	Methanol anhydrous, isobutanol, n-butanol	Sol clear; swells	Sol gels
	Ethanol, sec-butanol, octyl(2-ethylhexyl) alcohol	Sol clear; swells	Gels
	Isopropanol	Sol clear; swells	Swells
Monohydric cyclic alcohols	Cycohexanol	Gels	Sol clear
	Furfuryl alcohol, tetrahydro furfuryl acohol, methyl cyclohexanol	Sol clear	Gels
	Benzyl alcohol, phenyl ethyl alcohol	Sol clear	Sol clear
	Pine oil	Sol clear	Sol gels
Polyhydric alcohols	Ethylene glycol, diethylene glycol, glycerin	Insol	Insol
	Triethanolamine	Swells	Insol
Ethers	Ethyl ether, isopropylether, benzyl ether	Sol hazy	Swells
	Dioxane, morpholine	Sol clear	Sol clear
	n-butyl ether	Swells	Swells
	Phenyl ether	Swells	Sol hazy
C. ESTERS			
Acetates	Methyl acetate, ethyl acetate	Sol clear	Sol clear
	Isopropyl acetate, n-butyl acetate, cyclohexyl acetate	Sol gels	Sol clear
	Sec-butyl acetate, isobutyl acetate, glycol diacetate	Gels	Sol clear
	Sec-amyl acetate	Swells	Sol clear
Esters of hydroxy acids	Ethyl lactate, isopropyl lactate, methyl salicylate	Sol gels	Sol clear
	n-butyl lactate	Sol clear	Sol clear
D. KETONES			
Ketones	Acetone, methyl ethyl ketone	Sol clear; swells	Sol gels
	Methyl isobutyl ketone	Sol clear; swells	Swells
	Mesityl oxide, acetophenone	Sol clear	Sol gel
	Cyclohexanone, methyl cyclohexanone, diacetone alcohol	Sol clear	Gels

[a]solubility rated on a mixture of 2g ethocel in 18ml of solvent
Sol clear- soluble, solution clear of haze and free from gels
Sol hazy- soluble, solution hazy and free from gels
Sol gels- soluble, solution of granular nature due to presence of gels
Gels- completely gelatinized
Swells- swollen or incompletely gelatinized
Insol- insoluble

Choice of solvents for intermediate viscosities:
Solutions of ethyl cellulose polymers in aromatic hydrocarbons are highly viscous. Ethanol and methanol yield solution of ethyl cellulose polymers having lower viscosity than do aromatic hydrocarbons, but the properties of films are affected. There are mixtures of aromatic hydrocarbons with methanol or ethanol that yield solution of ethyl cellulose polymers having lower viscosity than is obtainable with either solvent type used singly. These mixtures also deposit films having good strength.

The low molecular weight aliphatic esters and ketones produce solutions of ethyl cellulose polymers that have comparatively low viscosities.

Table 10: Solvent composition for various solvent mixtures [16]

Solvent mixture	Solvent composition
Aromatic/ethanol	20% ethanol
Aromatic/ester	No change by varying ester
Esters/ethanol	20% ethanol
Ketones/ethanol	20% ethanol

C. Hydroxypropyl cellulose:
It is non-ionic water-soluble cellulose ether with a versatile combination of properties. It combines dual solubility in aqueous and polar organic solvents, thermoplasticity, and surface activity with the thickening and stabilizing properties, and can be used in tablet binding, modified release and film coating.

Chemistry of hydroxypropyl cellulose:

HPC (Fig 5) is an ether of cellulose in which some of the hydroxyl groups in the repeating glucose units have been hydroxypropylated forming $-OCH_2CH(OH)CH_3$ groups using propylene oxide.

The average number of substituted hydroxyl groups per glucose unit is referred to as the degree of substitution (DS). Complete substitution would provide a DS of 3. Because the hydroxypropyl group added contains a hydroxyl group, this can also be etherified during preparation of HPC. When this occurs, the number of moles of hydroxypropyl groups per glucose ring, moles of substitution (MS), can be higher than 3.

Because cellulose is very crystalline, HPC must have an MS of about 4 in order to reach a good solubility in water. HPC has a combination of hydrophobic and hydrophilic groups, so it has a lower critical solution temperature (LCST) at 45 °C. At temperatures below the LCST, HPC is readily soluble in water; above the LCST, HPC is not soluble.

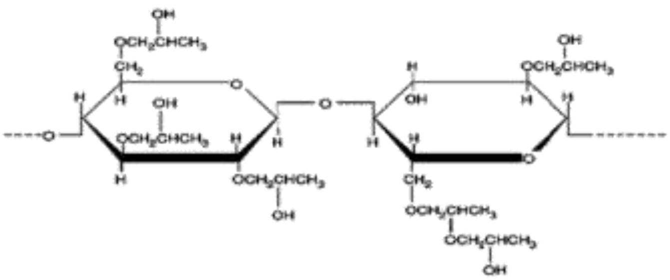


Figure 5: Chemical structure of hydroxypropyl cellulose

Nomenclature:
Hydroxypropyl cellulose is produced in several grades, determined by intended markets. For each grade, upto six viscosity types are available designated as H, M, G, J, L, E [25,26].

Intended market	Grade designation
Industrial	Industrial
Food	F
Personal care	CS
pharmaceutical	F pharm

Regular grind	Fine grind(or X)
HF pharm	HXF pharm
MF pharm	MXF pharm
GF pharm	GXF pharm
JF pharm	JXF pharm
LF pharm	--
EF pharm	EXF pharm

For example:
KLUCEL H X F pharm

F pharm → Intended for pharmaceutical purpose
X → Indicates finely ground grade
H → Indicates the viscosity grade

Table 11: Hydroxypropyl cellulose product grades

Different grades of HPC, their viscosities (cps) and corresponding molecular weights [25]-

I. Industrial grade

Viscosity types	Concentration in water by weight, %				Mol wt
	1	2	5	10	
H Industrial	1,275-3,500				1,150,000
M Industrial		3,500-7,500			850,000
G Industrial		125-450			370,000
J Industrial			125-450		140,000
L Industrial			65-175		95,000
E Industrial				250-800	80,000

II. Food grade

Viscosity types	Concentration in water by weight, %				Mol wt
	1	2	5	10	
GF		150-400			370,000
J F			150-400		140,000
LF			75-150		95,000
EF				200-600	80,000

III. Personal care grade, pharmaceutical grade

Viscosity types	Concentration in water by weight, %				Mol wt
	1	2	5	10	
H CS, HF pharm	1,500-3000				1,150,000
M CS, MF pharm		4000-6,500			850,000
G CS, GF pharm		150-400			370,000
J CS, JF pharm			150-400		140,000
L CS, LF pharm			75-150		95,000
E CS, EF pharm				300-600	80,000
Viscosity types	**Concentration in anhydrous alcohol by weight, %**				**Mol wt**
	1	**2**	**5**	**10**	
H CS, HF pharm	1000-4000				1,150,000
M CS, MF pharm		3000-6,500			850,000
G CS, GF pharm		75-400			370,000
J CS, JF pharm			75-400		140,000
L CS, LF pharm			25-150		95,000
E CS, EF pharm				150-700	80,000

All viscosities are determined at 25°C using Brookefield LVF viscometer with spindle and speed combinations depending on viscosity level.
Weight- average molecular weight determined by size exclusion chromatography.

Table 12: Description of hydroxypropyl cellulose products (USP specifications) [25,26]

Properties	Description
Physical appearance	White , essentially odorless and tasteless powder
Particle size: regular grind **Particle size: fine X-grind**	Min. 85% through 30 mesh Min. 99% through 20 mesh Industrial grade: Min. 80% through 30 mesh Min. 98% through 20 mesh Min. 80% through 100 mesh Min. 90% through 80 mesh Min. 99.9% through 60 mesh
Bulk Density, g/ml	0.5 (varies with type)
pH	Neutral to litmus (1% solution/water)
Softening temperature **Burn out temperature in N_2 or O_2**	100-150°C 450-500°C
Max. moisture content, (as packed)%	5.0
Specific gravity, g/cc (2% solution at 30°C)	1.010

Solubility:

Hydoxypropylcellulose is soluble in the broadest range of solvent systems: cold water, alcohol, and anhydrous systems (e.g., polar organic solvents and glycols). However HPC is generally insoluble in water over 105°F (40°C); however, this precipitation phenomenon occurs only in water and is fully reversible upon cooling.

HPC will precipitate from water solution at a temperature between 40ºC and 45ºC. This precipitation is completely reversible. The polymer redissolves upon cooling the system below 40ºC with stirring and the original is restored. When the temperature reaches 40 to 45ºC, this precipitation is evidenced by appearance of cloudiness in the solution and reduction in viscosity.

List of solvents for Hydroxypropyl cellulose [25]:

a) CLEAR AND SMOOTH

Glacial acetic acid	Ethyl alcohol	Propylene glycol
Acetone: water (9:1)	Formic acid 88%	t-butanol:water (9:1)
Benzene: methanol(1:1)	Glycerine: water(3:7)	Tetra hydro furan
Chloroform	Isopropyl alcohol 95%	Toluene: ethanol (3:2)
Cyclohexanone	Methanol	Water
Dimethyl formamide	Methylene chloride: methanol (9:1)	
Dimethyl sulphoxide	Morpholine	
Dioxane	Pyridine	

b) MODERATELY GRANULAR AND/OR HAZY

Acetone	Methyl acetate
Butyl acetate	Methyl ethyl ketone
Butyl cellosolve	Methylene chloride
Cyclohexanol	Naphtha:ethanol (1:1)
Isopropyl alcohol 99%	Tertiary butanol
Lactic acid	Xylene: isopropyl alcohol(1:3)

c) INSOLUBLE

Aliphatic hydrocarbon	Mineral oils
Benzene	Soyabean oil
Carbon tetrachloride	Toluene
Dichloro benzene	Gasoline
xylene	Glycerine
Trichloro ethylene	Linseed oil

D. Hydroxyethyl cellulose:

Hydroxy ethyl cellulose is a nonionic, water-soluble polymer that can thicken, suspend, bind, emulsify, form films, stabilize, disperse, retain water, and provide protective colloid action in a variety of pharmaceutical applications. It has outstanding tolerance for dissolved electrolytes. HEC offers narrow viscosity ranges, consistent viscosity reproducibility, and excellent solution clarities. Hydroxyethyl cellulose and methyl cellulose are frequently used with hydrophobic drugs in capsule formulations, to improve the drugs dissolution in the gastrointestinal fluids. This process is known as

"Hydrophilization".

Chemistry of hydroxyethyl cellulose:

Hydroxyethylcellulose polymer is hydroxyl-ethyl ether of cellulose. By treating cellulose with sodium hydroxide and reacting with ethylene oxide, hydroxyethyl groups are introduced to yield a hydroxyethyl ether. In this reaction, the hydrogen atoms in the hydroxyl groups of cellulose are replaced by hydroxyethyl groups, which confer water solubility to the product. The reaction product is purified and ground to a fine white powder. The maximum value for D.S. in hydroxyl ethyl cellulose is three [27].

In reacting ethylene oxide with cellulose to form the hydroxyethyl cellulose ether, solubility in water is achieved as the degree of substitution is increased. By selecting appropriate reaction conditions and moles of substituent, complete hydration in water is obtained. HEC, which has optimum solubility in water, has an MS of 2.5.

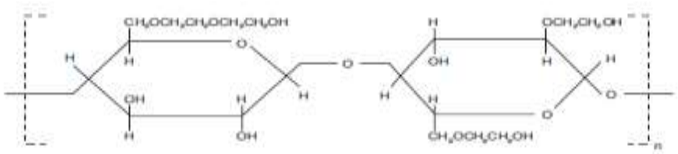


Figure 6: Chemical structure of hydroxyethyl cellulose

Nomenclature:
Two types of HEC are produced for specific dissolving purposes. QP type materials disperse rapidly, while WP types hydrate quickly. In addition, HEC is available in several grades, which have been specifically developed to improve their resistance to enzyme attack. They are designated ER type, enzyme resistant [28]. EP is primarily intended for use in emulsion polymerization. To offer longer self-life and protect cellulose ether from enzyme attack, WeKcelo HEC has Bio-stable grade available. These grades are designated by the letter B (e.g., WeKcelo HEC 30000B)

Hydroxyethyl cellulose product grades:

HEC is manufactured in a variety of viscosity grades. These versions differ principally in their aqueous solution viscosities and are offered to optimize performance in specific HEC applications. For a two-percent by weight aqueous solution, viscosities range from as low as 10 mPas up to 100,000 mPas.

Table 13: HEC Products for Industrial Applications [28,29]

CELLOSIZE DCS Grades	**Viscosity Range of Aqueous Solution, LVF Brookfield at 25°C, mPa•s**
CELLOSIZE DCS LV (170 KB PDF)	5000 (2% solution)
CELLOSIZE DCS HV (170 KB PDF)	50000 (2% solution)
CELLOSIZE EP Grades	
CELLOSIZE EP 09 hydroxyethyl cellulose	90-160 (5% solution)
CELLOSIZE EP 300 hydroxyethyl cellulose	250-400 (2% solution)
CELLOSIZE ER Grades	
CELLOSIZE ER 100M hydroxyethyl cellulose	3500-4400 (1% solution)
CELLOSIZE ER 15M hydroxyethyl cellulose	1100-1500 (1% solution)
CELLOSIZE ER 30M hydroxyethyl cellulose	1500-1900 (1% solution)
CELLOSIZE ER 37M hydroxyethyl cellulose	1900-2400 (1% solution)
CELLOSIZE ER 4400 hydroxyethyl cellulose	4800-6000 (2% solution)
CELLOSIZE ER 52M hydroxyethyl cellulose	2400-3000 (1% solution)
CELLOSIZE HEC Grades	
CELLOSIZE HEC-10 hydroxyethyl cellulose	4400-6500 (1% solution)
CELLOSIZE HEC-15 hydroxyethyl cellulose	50-80 (2% solution)
CELLOSIZE HEC-18 hydroxyethyl cellulose	250-400 (2% solution)
CELLOSIZE HEC-25 hydroxyethyl cellulose	4400-6500 (1% solution)
CELLOSIZE HEC-60 hydroxyethyl cellulose	180-325 (2% solution)
CELLOSIZE HEC-10 HV hydroxyethyl cellulose	>6000 (1% solution)
CELLOSIZE HEC-25 HV hydroxyethyl cellulose	>6000 (1% solution)
CELLOSIZE HMHEC Grades	
CELLOSIZE HMHEC 500 hydrophobe - modified hydroxyethyl cellulose	
CELLOSIZE QP Grades	
CELLOSIZE QP 09H hydroxyethyl cellulose	113-150 (5% solution)
CELLOSIZE QP 09L hydroxyethyl cellulose	75-112 (5% solution)
CELLOSIZE QP 10000H hydroxyethyl cellulose	
CELLOSIZE QP 15000H hydroxyethyl cellulose	1100-1500 (1% solution)
CELLOSIZE QP 100MH hydroxyethyl cellulose	4400-6000 (1% solution)
CELLOSIZE QP 100MHV hydroxyethyl cellulose	
CELLOSIZE QP 2000 hydroxyethyl cellulose	
CELLOSIZE QP 3L hydroxyethyl cellulose	215-282 (5% solution)
CELLOSIZE QP 300 hydroxyethyl cellulose	300-400 (2% solution)
CELLOSIZE QP 30000H hydroxyethyl cellulose	1500-2400 (1% solution)
CELLOSIZE QP 40 hydroxyethyl cellulose	80-125 (2% solution)
CELLOSIZE QP 4400H hydroxyethyl cellulose	4800-6000 (2% solution)
CELLOSIZE QP 52000H hydroxyethyl cellulose	2400-3000 (1% solution)
CELLOSIZE WP Grades	
CELLOSIZE WP 09H	113-150 (5% solution)

hydroxyethyl cellulose	
CELLOSIZE WP 09L hydroxyethyl cellulose	75-112 (5% solution)
CELLOSIZE WP 300 hydroxyethyl cellulose	
CELLOSIZE WP 52000H hydroxyethyl cellulose	
HEC Products for Oilfield Applications	
CELLOSIZE HEC-10 hydroxyethyl cellulose	4400-6500 (1% solution)
CELLOSIZE HEC-15 hydroxyethyl cellulose	50-80 (2% solution)
CELLOSIZE HEC-18 hydroxyethyl cellulose	250-400 (2% solution)
CELLOSIZE HEC-25 hydroxyethyl cellulose	4400-6500 (1% solution)
CELLOSIZE HEC-60 hydroxyethyl cellulose	180-325 (2% solution)
CELLOSIZE HEC-10 HV hydroxyethyl cellulose	>6000 (1% solution)
CELLOSIZE HEC-25 HV hydroxyethyl cellulose	>6000 (1% solution)
HEC Products for Personal Care Applications	
CELLOSIZE Polymer PCG-10	4400-6000 (1% solution)
CELLOSIZE QP 40 hydroxyethyl cellulose	80-125 (2% solution)
CELLOSIZE QP 300 hydroxyethyl cellulose	300-400 (2% solution)
CELLOSIZE QP 4400H hydroxyethyl cellulose	4800-6000 (2% solution)
CELLOSIZE QP 15000H hydroxyethyl cellulose	1100-1500 (1% solution)
CELLOSIZE QP 30000H hydroxyethyl cellulose	1500-2400 (1% solution)
CELLOSIZE QP 52000H hydroxyethyl cellulose	2400-3000 (1% solution)
CELLOSIZE QP 100MH hydroxyethyl cellulose	4400-6000 (1% solution)

Table 14: Description of hydroxyethyl cellulose products (USP specifications) [27,29]

Properties	Description
Physical appearance	White to cream-colored, freely flowing odourless granules or fine powder
Particle size	100% through U.S. 80 mesh (177 micron)
Bulk Density, g/cm³ **Apparent density, g/ml**	0.3-0.6 0.35-0.61
pH	6.0-8.5
Softening Point, °F (°C) **Decomposition Temperature, °F (°C)**	>285 (140) About 400 (205)
Viscosity(mpa.s), 20°C aqueous solution	5-60000
Specific Gravity at 20/20°C	1.30-1.40

Solubility:

The viscosity become little when the pH ranges from 2 to 12, but the viscosity reduces beyond this range. The HEC treated on the surface is soluble only when the pH is from 8 to 10.

Table 15: Solubility Behavior in Organic Solvents [27,29]

Solvent	Cold 25°C	Hot 55-60°C
Alcohols		
Ethanol:water (70:30 by wt)	Partially soluble	Partially soluble
(60:40 by wt)	Partially soluble	Partially soluble
(30:70 by wt)	Soluble	Soluble
Butanol	Insoluble	—
CARBITOL™ Solvent	Insoluble	—
Ethanol (95%)	Insoluble	—
Methyl CELLOSOLVE™ Solvent	Insoluble	—
Methanol	Insoluble	—
Glycols		
Ethylene glycol	Swollen	—
Glycerin	Swollen	Partially soluble
Propylene glycol	Swollen	Partially soluble
Acids		
Acetic Acid	Partially soluble	—
Glacial acetic	Insoluble	—
Formic Acid (90%)	soluble	—
Esters		
Amyl Acetate, Primary	Insoluble	—
Ethyl Acetate	Insoluble	—
Ethyl lactate	Insoluble	Insoluble
Methyl salicylate	Insoluble	Insoluble
Ethers		
Isopropyl Ether	Insoluble	—
Ethyl Ether	Insoluble	—
1,4-Dioxane	Insoluble	—
Methyl Cellosolve	Insoluble	—
Cellosolve	Insoluble	Insoluble
Hydrocarbons		
Xylene	Insoluble	—
Benzene	Insoluble	—
Petrolene	Insoluble	—
Kerosene	Insoluble	—
Chlorinated Hydrocarbons		
Chlorobenzene	Insoluble	—
Carbon Tetrachloride	Insoluble	—
Trichloroethylene	Insoluble	—
Ethylene Dichloride	Insoluble	—
Methylene Chloride	Insoluble	—
Aldehydes		
Butyraldehyde	Partially soluble	—
Formalin	soluble	—
Ketones		
Acetone	Insoluble	—
Diethyl Ketone	Insoluble	—

Amines		
Ethylenediamine	Soluble	—
Pyridine	Insoluble	—
Diethylenetriamine	soluble	—
Oils		
Mineral Oil	Insoluble	—
Cottonseed Oil	Insoluble	—
Lard Oil	Insoluble	—
Linseed Oil	Insoluble	—
Miscellaneous		
Dimethyl Formamide	Soluble	—
Dimethyl Acetamide	Soluble	—
Dimethyl Sulfoxide	Soluble	Soluble
Phenol	Soluble	Insoluble
Aniline	Insoluble	Soluble
Ethylene chlorohydrin	Soluble	

E. Carboxy methyl cellulose:

Carboxymethyl cellulose (CMC) or **cellulose gum** is a cellulose derivative with carboxymethyl groups ($-CH_2-COOH$) bound to some of the hydroxyl groups of the glucopyranose monomers that make up the cellulose backbone. It is often used as its sodium salt, sodium carboxymethyl cellulose. It is a low-cost commercial soluble and polyanionic polysaccharide derivative of cellulose.

Chemistry of Carboxymethyl cellulose:
The manufacture of CMC is a two-step process. In the first step, cellulose is suspended in alkali to open the bound cellulose chains, allowing water to enter. Cellulose is then reacted with sodium monochloroacetate to yield sodium carboxymethyl cellulose. The polar (organic acid) carboxyl groups render the cellulose soluble and chemically reactive by introducing carboxymethyl groups along the cellulose chain, which makes hydration of the molecule possible. The functional properties of CMC depend on the degree of substitution of the cellulose structure (i.e., how many of the hydroxyl groups have taken part in the substitution reaction), as well as the chain length of the cellulose backbone structure and the degree of clustering of the carboxymethyl substituents.

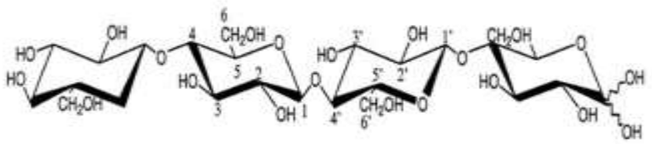


Figure 7: Chemical structure of Carboxymethyl cellulose

Nomenclature [30]:
An example of nomenclature for Hercules cellulose gum:
Cellulose gum type 7H3SXF

- The "7" stands for the degree of substitution. In the food industry, there are "7" and "9" types of substitution. The pharmaceutical industry also has a "1.2" type to work with.
- The "H" signifies a high viscosity grade, there are "L", "M", and "H" types, representing low, medium, and high viscosity respectively.
- "3" is a reference point which defines the maximum viscosity of the gum in a 1% solution at 25°C (in this case, 3000 centipoise).
- The "S" stands for special rheological properties (smooth flow). There are "S" types for smooth flow and "O" types for tolerance in acidic systems.
- The "X" stands for fine grind material, while a "C" would indicate a coarse particle size, and no letter would indicate a "regular" particle size.
- The "F" represents food grade (FCC), while a "P" would be pharmaceutical grade (USP).

Table 16: Carboxymethyl cellulose product grades [30,31]

Type	**Viscosity** (mPa s)
Hercules cellulose gum	
7LF	2% 25-50
7MF	2% 400-800
7HF	1% 1500-3000
9M8F	2% 400-800
9H4F	1% 2500-60000
Akucell cellulose gum	
Akucell AF 0305	1% 10–15 (Low viscosity)
Akucell AF 2785	1% 1500–2500 (Medium viscosity)
Akucell AF 3085	1% 8000–12000 (High viscosity)

Table 17: Description of Carboxymethyl cellulose products (USP specifications)

Properties	**Description**
Physical appearance	White to almost white, odorless, hygroscopic granular powder or fine fibres.
Bulk Density, g/cm³ **Tapped density, g/cm³**	0.52 g/cm³ 0.78
pH (1% w/v solution)	6.0-8.5
Melting point (°C)	Browns at approximately 227°C, and chars at Approximately 252°C.
Viscosity(mpa.s), 1% w/v aqueous solution	5–13 000 mPa s

Solubility:
CMC is practically insoluble in acetone, ethanol (95%), ether, and toluene. Easily dispersed in water at all temperatures forming clear colloidal solutions. The aqueous solubility varies with the degree of substitution (DS) (Number of carboxymethyl per glucose unit). The higher the DS, the higher the water solubility, pH resistance, salt compatibility etc. Cellulose gum (CMC) is also soluble in most aqueous mixes such as alcohol/water, glycerine/water etc. When other solutes such as salts are added, it is recommended to dissolve the cellulose gum first.

APPLICATIONS AND ADVANTAGES OF CELLULOSE POLYMERS

Polymers offer an outstanding range of controlled release properties for a wide variety of dosage forms and processing methods.

1. **Methyl cellulose and Ethyl cellulose:** In pharmaceuticals, Methyl cellulose has principle advantages of formulation versatility and the ability to "fine tune", improving product appearance, i.e., tablet physical properties and helps to assure the customer acceptance [32]. Ethyl cellulose has excellent compatability with wide variety of pharmaceutical systems incorporating an even greater number of basic ingredient materials and are used where hydrophobic films are needed.

Table 18: Applications of methyl and ethyl cellulose [8,12]

Application	Products Recommended	Typical Use Level
Controlled Release Applications		
Controlled Release Matrix Tablets	METHOCEL K100LV, K4M, K15M, K100M, E4 M, E10M Premium (all available in Controlled Release, CR grade)	20 – 55%
Controlled Release Coatings	ETHOCEL Standard Premium 4,7,10 ETHOCEL Premium blended with METHOCEL E5, E15 Premium	3 – 20% 3 – 20%
Microencapsulation	ETHOCEL Standard 20, 45, 100 Premium	10 – 20%
Tablet Coating Applications		
Conventional Tablet Coating	METHOCEL E3, E5, E6, E15LV Premium	0.5 – 5%
Solvent-Based Coating for Barrier or Taste Masking Properties	Blends of ETHOCEL Premium and METHOCEL Premium	1 – 5%
Granulation Binder Applications		
Conventional Wet Granulation	METHOCEL E5LV, E15LV, A15LV, K3 Premium	2 – 6%
Direct Compression Granulation	ETHOCEL Standard 7 FP, 10 FP, 100 FP Premium	5 – 40%
Solvent-Based Granulation	ETHOCEL Standard 10, 20 or 45 Premium	1 – 6%
Liquid Formulations		
Bulk laxatives	METHOCEL A4M, K4M, K100M Premium	5 – 30%
Creams, gels, and ointments	METHOCEL A4M, E4M, F4M, K4M Premium	1 – 5%
Ophthalmic preparations	METHOCEL E4M Premium	0.1 – 0.5%
Suspensions	METHOCEL A4M, E4M, K4M Premium	1 – 2%
Antacids	METHOCEL A15C, A4M, E4M, K4M, K15M, F4M Premium	1 – 2%

Table 19 Summarizes the recommendations for METHOCEL products to be used with selected granulation processes and active ingredients [10,33,34,35].

S.NO	Active Ingredient	METHOCEL Product
1	High-dose, low-solubility drug	A15 Premium LV; E5 Premium LV
2	High-dose, high-solubility drug	E5 Premium LV; K3 Premium LV
3	Low-dose, low-solubility drug	A15 Premium LV; K3 Premium LV; E5 Premium LV
4	High-dose, high-solubility drug	A15 Premium LV; K3 Premium LV; E5 Premium LV; E15 Premium LV

1, 2&3-------- Recommended granulation process is Low- and high-shear granulation; fluid-bed granulation
4--------------- Recommended granulation process is roller-compaction granulation

2. **Hydroxy propyl cellulose:** The breadth of viscosity grades of HPC can be used for wide ranging applications. As a food additive, hydroxypropyl cellulose is used as a thickener and as an emulsion stabilizer. Lacrisert, manufactured by Aton Pharma, is a formulation of HPC used for artificial tears. It is used to treat medical conditions characterized by insufficient tear production such as keratoconjunctivitis sicca , recurrent corneal erosions, decreased corneal sensitivity, exposure and neuroparalytic keratitis. HPC is also used as a lubricant for artificial eyes. HPC is used as a sieving matrix for DNA separations by capillary and microchip electrophoresis.

Table 20: Applications of hydroxypropyl cellulose [25]

Types of uses	Specific applications	Properties utilized
Adhesive	Solvent-based hot-melt	Thickener, thermoplastic
Aerosol	Emulsions-cosmetics	Stabilizer, foaming aid
	Solvent based	Film former, binder
Coatings	Edible food coating	Glaze-oil and oxygen barrier
	Film coating	Solvent-soluble film former, heat sealable
Cosmetics	Hair styling aids, alcohol based preparations, perfumes, etc.	Alcohol soluble thickener, and film former
	Emulsions, creams, lotions and shampoos	Emulsion stabilizer, thickener

Encapsulation	Micro and macro encapsulation	Soluble, edible, flexible film barrier, fast release
Extrusion	Film and sheet profiles and filaments	Thermoplastic, binder, water and solvent soluble
Molding	Injection, compression and blow molding	Thermoplastic, binder, water and solvent soluble
Pharmaceuticals	Tablet binder, tablet coating, modified release liquids and semi solids.	Aqueous and solvent solubility, thermoplastic binder, non-ionic, pH-insensitive thickener, suspending agent, diffusion barrier, flexible films

3. **Hydroxyethyl cellulose:** It can be used in a variety of industrial and pharmaceutical applications, including as a lubricant in preparations for dry eye, contact lens care, and dry mouth.

Table 21: Applications of Hydroxyethyl cellulose [9,36]

Types of uses	Specific applications	Properties utilized
Coating	Latex paint Texture paint	Thickening and protective colloid, Water-binding
Cosmetics	Hair conditioners Toothpaste Liquid soaps and bubble bath Hand creams and lotions	Thickening and stabilizing
Adhesives	Wallpaper adhesives Latex adhesives Plywood adhesives	Thickening, lubricity, water-binding and solids holdout
Pharmaceuticals	Lotions and emulsions Jellies and ointments	Thickening, stabilizing and water-binding
	Ophthalmic and topical formulations	Thickening agent
	Tablets	Binder and film coating agent
Polymerization	PVAC and acrylic latices PVC suspension	Protective colloid and surface activity
Industry	Paper, Textiles, Laundry Aids, Binders	Adhesives, decorative and protective coatings, emulsion polymerization
Miscellaneous	Joint cements Hydraulic cements Plaster Caulking compound and putty Printing inks Asphalt emulsions	Thickening, water-binding, set retarder, rheology control, stabilizing, protective coating and polymerization

4. **Carboxymethyl cellulose:** Carboxymethyl cellulose sodium is widely used in oral and topical pharmaceutical formulations, primarily for its viscosity increasing properties. CMC is used as a lubricant in non-volatile eye drops (artificial tears) and also used in cosmetics, toiletries, surgical prosthetics, and incontinence, personal hygiene, and food products.

Table 22: Applications of Carboxy methyl cellulose [31, 37]

Types of uses	Specific applications	Properties utilized
Adhesive	Denture adhesive	Wet tack, long lasting adhesion
Pharmaceuticals	Tablet binder, granulation aid	High strength binder
	Sustained release	Thickener, diffusion barrier
	Tablets	Film former, disintegrant
	Syrups and suspensions	Thickener, suspending aid
	Bulk laxative	Physiologically inert, high water binding capacity
Cosmetics	Shampoos, foamed products, creams, lotions, tooth paste	Foam stabilizer, suspending aid, thickener, film former, binder

Conclusion

The drug development business has become truly global, especially in the area of procurement of components, outsourcing of manufacture, and global commercialization. The emergence of controlled release technology as an effective way to enhance patient compliance and extend the life cycle of a drug has led to the need for novel ways of controlling the drug release profiles. Polymers present a logical and simple approach to control the release of drugs and also play a key role in optimizing the therapeutic delivery of drug. The text fulfills a critical need for up-to-date and comprehensive information about a rapidly evolving area of interest. We encourage readers to learn from this text and to consider themselves challenged in helping pharmaceutical scientists "what to do and what not to do" when selecting a suitable polymer for a specific dosage form.

A deeper understanding of polymer properties and its impact on dosage form functionality is further going to fuel this trend. Uneducated selection of polymer likely leads to numerous formulating flaws that require much time and materials. It is therefore logical to select polymers by their properties when designing or optimizing a formulation, and knowledge of polymer properties is an important prerequisite for this process. Selecting polymers with properties that complement the poor qualities of an API or formulation is often an appropriate first step. Finally, knowledge of polymer properties is essential in creating a robust formulation to manufacture a dosage form that meets specifications in a time and material efficient manner.

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Conflict of Interest

The authors report no conflicts of interest.

References

1. Hinterstoisser B., Salmen L. Application of dynamic 2D FTIR to cellulose. Vibrational Spectroscopy, 2000; **22**: 111–118.
2. Bochek A. M. Effect of hydrogen bonding on cellulose solubility in aqueous and nonaqueous solvents. Russian Journal of Applied Chemistry, 2003; **76**: 1711– 1719.
3. Myasoedova V. V. Physical chemistry of non-aqueous solutions of cellulose and its derivatives. John Wiley and Sons, Chirchester 2000.
4. Gross R. A., Scholz C. Biopolymers from polysaccharides and agroproteins. American Chemical Society, Washington 2000.
5. Akira .I. Chemical modification of cellulose. In 'Wood and Cellulosic Chemistry' (eds., Hon D. N-S., Shiraishi N.) Marcel Dekker, New York, 2001; 599–626.
6. S. Kamel, N. Ali, K. Jahangir, S. M. Shah, A. A. El-Gendy. Pharmaceutical significance of cellulose: A review. eXPRESS Polymer Letters, 2008; Vol.2, No.11: 758–778.
7. J. B. Batdorf and P.S.Francls. The Physical Behavior of Water-Soluble Cellulose Polymers. Journal of the Society of Cosmetic Chemists, 1962; 117-122.
8. An introduction to Dow Pharmaceutical Excipients: An Expanding World of Solutions through Science and Polymer Technology; Published literature by Dow chemicals, Form No. 198-02141 1005.
9. Technical handbook of Methocel cellulose ethers; Published literature by Dow chemicals, Form No: 192-01062-0902, 2002.
10. Sheskey, P.J., and T.P. Dasbach, Evaluation of various polymers as dry binders in the preparation of an immediate-release tablet formulation by roller compaction; *Pharm. Technol.* 1995; **19** (10): 98–112.
11. Foam enhancement, thickening, gelling, film formation, and stabilization, Methocel cellulose ethers: Multi functional water-soluble polymers that enhance foams, forms films, thicken and stabilize; Amerchol, The elegance engineers; Form No: 324-00180-0805, 2005; 1-31.
12. Information brochure of Pharmaceutical Excipients from Dow Water Soluble Polymers: A broad line of products and technologies from a single supplier to help you maximize performance faster; Dow chemicals, Form No. 198-02088-0802, 2002.
13. Paul J. Sheskey, Tim D. Cabelka, Ryan T. Robb, and Brent M. Boyce; Product Information, Use of Roller Compaction in the Preparation of Controlled-Release Hydrophilic Matrix Tablets Containing Methylcellulose and Hydroxypropyl Methylcellulose Polymers; Reprinted from *Pharmaceutical Technology*, an ADVANSTAR Publication,1994; 1-12.
14. Introducing METHOCEL™ DC Grade Hypromellose Polymers for Direct Compression of Controlled Release Dosage Forms: Achieve Excellent Processing, Physical Properties and Dissolution Profiles without the Need for Wet Granulation; published literature by DowWolf Cellulosics, Form No. 198-02173-1008, 2008.
15. Ethocel premium polymers for pharmaceutical applications: Proven organosoluble polymers for controlled release coatings, microencapsulation, granulation and flavor markings; Form No: 198-02002-1098, 1998.
16. Dow Cellulosics, Technical Handbook of ETHOCEL Ethyl cellulose polymers, Form No: 192-00818-0905, 2005.
17. Majewicz, T.G. "Cellulose ethers," Encyclopedia of polymer science and technology, John Wiley & Sons, Inc., New York, 2002.
18. Kent, D.J., and Rowe, R.C. Solubility studies on ethyl cellulose used in film coating. J. Pharm. Pharmacol., 1978; 30: 808-810.
19. Rowe, R.C. The prediction of compatibility/incompatibility in blends of ethyl cellulose with hydroxypropyl methylcellulose or hydroxypropyl cellulose using 2-dimensional solubility parameter maps. J. Pharm. Pharmacol., 1986; 38: 214-5.
20. Sakellariou, P., Rowe, R.C., and White. The solubility parameters of some cellulose derivatives and polyethylene glycols used in tablet film coating. Int. J. Pharm., 1986; 31: 175-7.
21. Arwidsson, H., and Nicklasson, M. Application of intrinsic viscosity and interaction constant as a formulation tool for film coating. I. Studies on ethyl cellulose 10 cps in organic solvents. International Journal of Pharmaceutics, 1989; 56: 187-193.
22. Robinson, D.H. Ethyl cellulose-solvent phase relationships relevant to coacervation microencapsulation processes. Drug Dev. Ind. Pharm., 1989; 15: 2597-2620.
23. Arwidsson, H., and Nicklasson, M., Int. J. Pharm., 1990, 58, 73-7.
24. Archer, W.L. Determination of Hansen solubility parameters for selected cellulose ether derivatives. Ind. Eng. Chem. Res. 1991; 30: 2292-2298.
25. Klucel® Hydroxy propyl cellulose: Physical and chemical properties, Hercules incorporated, Aqualon division, 2001.

26. Product data, KLUCEL® Pharm Hydroxypropylcellulose; Hercules incorporated, Aqualon division, Number 494-9, 2004.
27. WeKcelo™ HEC: Hydroxyethylcellulose, A Nonionic Water-Soluble Polymer: WeKcelo ™HEC and Its Applications; Information brochure by WeiKem Chemicals, 2009; 1-12.
28. CELLOSIZE Hydroxyethyl Cellulose for Coatings Applications: High Thickening Efficiency, Excellent Formulation Compatibility, and Available with Superior Enzyme Resistance, Form No. 325-00002-1002, 2002.
29. CELLOSIZE Hydroxyethyl Cellulose: Thickener, Binder, Stabilizer, Film Former, Protective Colloid, Information brochure by Dow chemicals, Form No. 325-00001-0805, 2005; 1-27.
30. Andrew C. Hoefler; Sodium Carboxymethyl Cellulose: Chemistry, Functionality, and Applications; Food Ingredients Group, Hercules Incorporated Wilmington, Delaware 19808, 1-15.
31. Raymond C Rowe, Paul J Sheskey and Sian C Owen , Handbook of Pharmaceutical Excipients; Fifth edition, 2006.
32. Information brochure of METHOCEL Cellulose Ethers in Aqueous Systems for Tablet Coating; Dow chemicals, Form No. 198-00755-0702, 2002.
33. The Dow Chemical Company, Technotes: Granulation with Cellulosic Polymers, Part I. Fluid Bed Granulation; Form No. 198-01151-0702; 24pp.
34. The Dow Chemical Company, Technotes: Granulation with Cellulosic Polymers, Part II. High Shear Granulation; Form No. 198-01170-0702; 28pp.
35. The Dow Chemical Company, Technotes: Granulation with Cellulosic Polymers, Part III. Low Shear Granulation; Form No. 198-01181-0602; 27pp.
36. Aqualon, Specialties, Natrosol® hydroxyethylcellulose, http://www.herc.com/aqualon/specialties/products/spec_prod_nathec.html, 2005.
37. Hercules Incorporated, Aqualon Division: http://www.aqualon.com (16.07.2008).