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**Review Article** 

ISSN 2045-080X



#### **Basic Concepts Of Cellulose Polymers- A Comprehensive Review**

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**Citation:** Harika K, Sunitha K, Pavan Kumar P, Maheshwar K and Madhusudan Rao Y. **Basic Concepts Of Cellulose Polymers- A Comprehensive Review.** Archives of Pharmacy Practice. 2012; 3(3)pp202-216.

#### 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,

#### **Key words**

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Cellulose Polymers, Premium Product Grades, Viscosities, Solubility.

#### **Manuscript History**

Article Received on: 1<sup>st</sup> Jan, 2012 Revised on: 30<sup>th</sup> April, 2012 Approved for Publication: 10<sup>th</sup> June, 2012

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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.

#### 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).



**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).

ROH	+	R'CI	$\rightarrow$	ROR'	+	HCI	
alcohol	al	kylchlor	ide	ether	hyd	lrogen chloride	

Equation 1: Etherification of cellulose. R'= organic radical (CH<sub>3</sub>-, C<sub>2</sub>H<sub>5</sub>-, etc)

Table 1:	Ether	derivatives	[6,7]	
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Cellulose	Reagent	Example	Reagent
ethers			
Alkyl	Halogeno	Methylcellulose	Chloromethane
	alkanes	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	Reagent	Example	Reagent
Organic	Organic	Cellulose	Acetic acid and
esters	acius	acetate	acetic annyuride
		Cellulose	Acetic acid and
		triacetate	acetic anhydride
		Cellulose	Propanoic acid
		propionate	
		Cellulose	Acetic acid and
		acetate	propanoic acid
		propionate	
		Cellulose	Acetic acid and
		acetate	butyric acid
		butyrate	
Inorganic	Inorganic	Nitrocellulose	Nitric acid or
esters	acids	(cellulose	another
		nitrate)	powerful
		-	nitrating agent
		Cellulose	Sulfuric acid or
		sulfate	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.

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

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

#### 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].



R = CH, in approx 2/3 of the case, H otherwise

#### Figure 2: Chemical structure of methyl cellulose



Figure 3: Chemical Structure of Hydroxypropyl 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

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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

Product	Chemica	Available	Meth	Hydr	Avg
	l type	viscosities	oxy	oxypr	particle
		, cps	%	opyl	size
				%	(µm)
Methocel	Methyl	15, 400,	27.5-	0	85.6
Α	cellulose	1,500,	31.5		
premium	USP	4,000			
Methocel	Hyprom	3, 5, 6, 15,	28.8-	7-12	72.2
Е	ellose	50, 400,	30		
premium	2910	10,000			
Methocel	Hyprom	50, 4,000	27-	4-7.5	65
F	ellose		30		
premium	2906				
Methocel J			16.5-	23-32	88.4
premium			20		
Methocel	Hyprom	3, 100,	19-	4-12	64.7
К	ellose	4,000,	25		
premium	2208	15,000			
		1,00,000			
Methocel			25	25	100-500
310 series					

. . . . . . . . .

- METHOCEL E Premium products are also available in  $\geq$ 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  $\triangleright$ 2% solutions in H<sub>2</sub>O at  $20^{\circ}$ C

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

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

#### Solubility:

 $\geq$ 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  $\triangleright$ equal volumes of ethanol and chloroform.
- $\triangleright$ 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 I cellulose ether products possess structures that provide unusual solubility properties. They are soluble in certain nonaqueous media at elevated temperatures. ,,

Table 6:	Examples of suitab	le "hot solvents
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Solvent	Boiling	Solubility	Degree of
	point °C	point °C	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	127	100	Completely soluble
monoacetate			
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 organo-soluble family of а 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	Viscosi	Ethoxyl cont	Mean	
viscosity	tv	Std	Med	partic
designation	range	500		le
	mPa.s			size
	(cP)			(µm)
ETHOCEL Std	3-5.5	48.0-49.5%		
4 premium				
ETHOCEL Std	6-8	48.0-49.5%		310.0
7 premium				
ETHOCEL Std	6-8	48.0-49.5%		5.0-
7FP premium				15.0
ETHOCEL Std	9-11	48.0-49.5%		375.0
10 premium				
ETHOCEL Std	9-11	48.0-49.5%		3.0-
10FP premium				15.0
ETHOCEL Std	12.6-	48.0-49.5%		
14 premium <sup>a</sup>	15.4			
ETHOCEL Std	18-22	48.0-49.5%		
10 premium				
ETHOCEL Std	41-49	48.0-49.5%		
45 premium				
ETHOCEL Med	45-55		45.0-46.5%	
50 premium <sup>a</sup>				
ETHOCEL Med	63-77		45.0-46.5%	
70 premium <sup>a</sup>				
ETHOCEL Std	90-110	48.0-49.5%	45.0-46.5%	465.0
100 premium <sup>a</sup>				
ETHOCEL Std	90-110			30-60
100FP				
premium				
ETHOCEL Std	180-	48.0-49.5%		
200 premium	220			
ETHOCEL Std	270-	48.0-49.5%		
300 premium	330			

(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
produ	cts (	USP specifica	tior	ıs) [17]		

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

#### 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 ofcommon single solvents [16]

Solvent		Solubility <sup>a</sup> ceullulose	of ethyl polymers
A. HYDR	OCARBONS		p <b>j</b>
Туре	Name of solvent	Standard ethoxyl	Medium ethoxyl
Aromatic	Toluene, xylene	Sol clear	Gels
hydrocarbons	Ethyl benzene	Sol clear	Sol gels
	Isopropyl benzene	Sol clear	Swells
	Diethyl benzene,	Sol gels	Swells
	diphenyl ethane	_	
Cyclo	Cyclo hexane,	Swells	Insol
aliphatic	methyl cyclohexane		
hydrocarbons	Cyclo hexene	Sol clear	Sol clear
Chlorinated	Chloroform,	Sol clear	Sol clear
aliphatic	ethylene dichloride,		
hydrocarbons	trichloro ethylene,		
	propylene		
	dichloride, trichloro		
	ethane, tetrachloro		
	ethane, methylene		
	chloride		
	Carbon tetra	Sol clear	Gels
	chloride		
	Perchloroethylene	Sol hazy	Swells
Chlorinated	Monochloro	Sol clear	Sol hazy
aromatic	benzene, o-dichloro		
hydrocarbons	benzene		
	Trichloro benzene	Sol clear	Swells
B. ALCO	HOLS AND ETHERS		1
Monohydric	Methanol	Sol clear;	Sol gels
aliphatic	anhydrous,	swells	
alcohols	isobutanol, n-		
	butanol		
	Ethanol, sec-	Sol clear;	Gels
	butanol, octyl(2-	swells	
	ethylhexyl) alcohol		0 11
	Isopropanol	Sol clear;	Swells
Manah 11	Caraliana	Swells	
Monohyaric		Gels	Sol clear
cyclic	ruriuryi alconol,	Sol clear	Gels
alconois	tetranyaro furfuryl		
	aconol, methyl		
	Cyclollexanol Rongul alash-1	Solalaar	Colobert
	phonyl alcohol,	Sol clear	Sol clear
	alcohol etnyi		
	alconol		

	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. ESTE	RS		
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. KETO	NES		
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

<sup>a</sup>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]

[=0]	
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

<b>Regular grind</b>	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:



#### 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	
Н	1,275-				1,150,000
Industrial	3,500				
М		3,500-			850,000
Industrial		7,500			
G		125-			370,000
Industrial		450			
J			125-		140,000
Industrial			450		
L			65-		95,000
Industrial			175		
Е				250-	80,000
Industrial				800	

II. Food grade

Viscosity types	Co	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

Viscosity	y	Conc	Mol wt			
types						
		1	2	5	10	
H CS,	HF	1,500-				1,150,000
pharm		3000				
M CS, I	MF		4000-			850,000
pharm			6,500			
G CS,	GF		150-			370,000
pharm			400			
J CS,	JF			150-		140,000
pharm				400		
L CS,	LF			75-		95,000
pharm				150		
E CS,	EF				300-	80,000
pharm					600	
F -						
Viscosity	y	Conce	ntration	in anhyd	rous	Mol wt
Viscosity types	y	Conce alc	ntration i	in anhyd weight, 9	rous %	Mol wt
Viscosity types	у	Conce alc 1	ntration cohol by 2	in anhyd weight, 9 5	rous % 10	Mol wt
Viscosity types H CS,	y HF	Conce alc 1 1000-	ntration cohol by 2	in anhyd weight, 9 5	rous % 10	<b>Mol wt</b> 1,150,000
Viscosity types H CS, pharm	y HF	Conce ald 1 1000- 4000	ntration cohol by 2	in anhyd weight, 9 5	rous % 10	<b>Mol wt</b> 1,150,000
Viscosity types H CS, pharm M CS,	y HF MF	Conce alo 1 1000- 4000	ntration cohol by 2 3000-	in anhyd weight, 9 5	rous % 10	Mol wt 1,150,000 850,000
Viscosity types H CS, pharm M CS, I pharm	y HF MF	Conce alo 1 1000- 4000	ntration 2 2 3000- 6,500	in anhyd weight, 9 5	rous % 10	<b>Mol wt</b> 1,150,000 850,000
Viscosity types H CS, pharm M CS, H pharm G CS,	y HF MF GF	Conce ald 1 1000- 4000	ntration 2 3000- 6,500 75-	in anhyd weight, 9 5	rous % 10	Mol wt 1,150,000 850,000 370,000
Viscosity types H CS, pharm M CS, H pharm G CS, pharm	y HF MF GF	Conce ald 1 1000- 4000	ntration 2 3000- 6,500 75- 400	in anhyd weight, <sup>o</sup> 5	rous % 10	Mol wt 1,150,000 850,000 370,000
Viscosity types H CS, pharm M CS, I pharm G CS, pharm J CS,	y HF MF GF JF	Conce ald 1000- 4000	ntration 2 2 3000- 6,500 75- 400	in anhyd weight, 9 5 75-	rous % 10	Mol wt 1,150,000 850,000 370,000 140,000
Viscosity types H CS, pharm M CS, J pharm G CS, pharm J CS, pharm	y HF MF GF JF	Conce ald 1000- 4000	ntration 2 2 3000- 6,500 75- 400	in anhyd weight, 9 5 75- 400	rous // 10	Mol wt           1,150,000           850,000           370,000           140,000
Viscosity types H CS, pharm M CS, pharm G CS, pharm J CS, pharm L CS,	y HF MF GF JF LF	Conce ald 1 1000- 4000	ntration 2 2 3000- 6,500 75- 400	in anhyd weight, 9 5 75- 400 25-	rous // 10	Mol wt 1,150,000 850,000 370,000 140,000 95,000
Viscosity types H CS, pharm M CS, H pharm G CS, pharm J CS, pharm L CS, pharm	y HF MF GF JF LF	Conce ald 1 1000- 4000	<b>ntration</b> <b>2</b> 3000- 6,500 75- 400	n anhyd weight, 9 5 75- 400 25- 150	rous // 10	Mol wt         1,150,000         850,000         370,000         140,000         95,000
Viscosity types H CS, pharm M CS, P pharm G CS, pharm J CS, pharm L CS, pharm E CS,	y HF GF JF LF EF	Conce ald 1000- 4000	ntration 2 2 3000- 6,500 75- 400	in anhyd weight, 9 5 75- 400 25- 150	10 10	Mol wt         1,150,000         850,000         370,000         140,000         95,000         80,000

III. Personal care grade, pharmaceutical grade

# 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	Min. 85% through 30 mesh
	Min. 99% through 20 mesh
	Industrial grade:
	Min. 80% through 30 mesh
	Min. 98% through 20 mesh
Particle size: fine X-grind	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)
рН	Neutral to litmus (1%
	solution/water)
Softening temperature	100-150°C
Burn out temperature in N <sub>2</sub> or	450-500°C
02	
Max. moisture content, (as	5.0
packed)%	
Specific gravity, g/cc (2%	1.010
solution at 30°C)	

#### 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  $40^{\circ}$ C and  $45^{\circ}$ C. This precipitation is completely reversible. The polymer redissolves upon cooling the system below  $40^{\circ}$ C with stirring and the original is restored. When the temperature reaches 40 to  $45^{\circ}$ C, 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 S	MOOTH			
Glacial acetic acid	Ethyl alc	ohol	Propylene	glycol
Acetone: water	Formic	acid	t-butanol:	water
(9:1)	88%		(9:1)	
Benzene:	Glycerine	5:	Tetra hydi	o furan
methanol(1:1)	water(3:	7)		
Chloroform	Isopropy	l	Toluene:	ethanol
	alcohol 9	5%	(3:2)	
Cyclohexanone	Methano	1	Water	
Dimethyl	Methyler	ne	chloride:	
formamide	methano	l (9:1)		
Dimethyl	Morphol	ine		
sulphoxide				
Dioxane	Pyridine			
b) MODERATEL	Y GRANU	LAR AN	D/OR HAZY	
Acetone	М	ethyl ac	etate	
Butyl acetate	Μ	ethyl et	hyl ketone	
Butyl cellosolve	Μ	ethylen	e chloride	
Cyclohexanol	Ν	aphtha:	ethanol (1:1)	
Isopropyl alcohol 9	9% T	ertiary ł	outanol	
Lactic acid	X	ylene: is	opropyl alco	hol(1:3)
c) INSOLUBLE				
Aliphatic hydrocarb	on	Μ	ineral oils	
Benzene		Sc	oyabean oil	
Carbon tetrachlorid	e	Т	oluene	
Dichloro benzene		Ga	asoline	
xylene		G	lycerine	
Trichloro ethylene		Li	nseed 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 Biostable 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	250-400 (2% solution)		
cellulose	250-400 (2% solution)		
CELLOSIZE ER Grades			
hydroxyethyl cellulose	3500-4400 (1% solution)		
CELLOSIZE ER 15M hydroxyethyl	1100-1500 (1% solution)		
cellulose	1100 1000 (17,0 5010001)		
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	2400,2000,(10),		
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	>6000 (1% solution)		
hydroxyethyl cellulose			
hydroxyethyl cellulose	>6000 (1% solution)		
CELLOSIZE HMHEC Grades			
CELLOSIZE HMHEC 500 hydrophol	oe - modified hydroxyethyl		
CELLOSIZE OP Grades			
CELLOSIZE QP 09H hydroxyethyl cellulose	113-150 (5% solution)		
CELLOSIZE QP 09L hydroxyethyl	75-112 (5% solution)		
CELLOSIZE OP 10000H bydrovyeth			
CELLOSIZE OP 15000H			
hydroxyethyl cellulose	1100-1500 (1% solution)		
CELLOSIZE QP 100MH	4400-6000 (1% solution)		
CELLOSIZE OP 100MHV hydroxyet	hyl cellulose		
CELLOSIZE OP 2000 hvdrovvethvl	rellulose		
CELLOSIZE QP 3L hydroxyethyl	215-282 (50% colution)		
cellulose	213-202 (3%) SOIUUOIIJ		
CELLOSIZE QP 300 hydroxyethyl cellulose	300-400 (2% solution)		
CELLOSIZE QP 30000H hvdroxyethyl cellulose	1500-2400 (1% solution)		
CELLOSIZE QP 40 hydroxyethyl cellulose	80-125 (2% solution)		
CELLOSIZE QP 4400H	4000 6000 (20/		
hydroxyethyl cellulose	4000-0000 (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	75,112 (50/ colution)	
cellulose	73-112 (3% solution)	
CELLOSIZE WP 300 hydroxyethyl o	cellulose	
CELLOSIZE WP 52000H hydroxyet	hyl cellulose	
HEC Products for Oilfield Applica	ations	
CELLOSIZE HEC-10 hydroxyethyl	4400,6500,(106,colution)	
cellulose	4400-8300 (1% solution)	
CELLOSIZE HEC-15 hydroxyethyl	50.80(20%  solution)	
cellulose	30-80 (2% solution)	
CELLOSIZE HEC-18 hydroxyethyl	250,400,(206,colution)	
cellulose	230-400 (2%) solution	
CELLOSIZE HEC-25 hydroxyethyl	4400-6500 (1% solution)	
cellulose	4400-0500 (1% solution)	
CELLOSIZE HEC-60 hydroxyethyl	180-325 (2% solution)	
cellulose	100-325 (2%) solution	
CELLOSIZE HEC-10 HV	>6000 (1% solution)	
hydroxyethyl cellulose	20000 (1% solution)	
CELLOSIZE HEC-25 HV	>6000 (1% solution)	
hydroxyethyl cellulose	20000 (1% solution)	
HEC Products for Personal Care	Applications	
CELLOSIZE Polymer PCG-10	4400-6000 (1% solution)	
CELLOSIZE QP 40 hydroxyethyl	80-125 (20% solution)	
cellulose	00-125 (2% solution)	
CELLOSIZE QP 300 hydroxyethyl	300-400 (2% solution)	
cellulose	500-400 (2 % solution)	
CELLOSIZE QP 4400H	4800-6000 (2% solution)	
hydroxyethyl cellulose		
CELLOSIZE QP 15000H	1100-1500 (1% solution)	
hydroxyethyl cellulose	1100-1300 (170 solution)	
CELLOSIZE QP 30000H	1500-2400 (1% solution)	
hydroxyethyl cellulose	1300-2400 (170 Solution)	
CELLOSIZE QP 52000H	2400-3000 (1% solution)	
hydroxyethyl cellulose		
CELLOSIZE QP 100MH	4400-6000 (1%  solution)	
hydroxyethyl cellulose		

### 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/cm <sup>3</sup>	0.3-0.6	
Apparent density, g/ml	0.35-0.61	
рН	6.0-8.5	
Softening Point, °F (°C)	>285 (140)	
Decomposition		
Temperature, °F (°C)	About 400 (205)	
Viscosity(mpa.s), 20°C 5-60000		
aqueous solution		
Specific Gravity at	1.30-1.40	
20/20°C		

#### 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	1	1	
Ethanol:water (70:30 by wt)	Partially	Partially	
	soluble	soluble	
(60:40 by wt)	Partially	Partially	
	soluble	soluble	
(30:70 by wt)	Soluble	Soluble	
Butanol	Insoluble	—	
CARBITUL <sup>™</sup> Solvent	Insoluble	—	
Ethanol (95%)	Insoluble	_	
Methyl CELLOSOLVE	Insoluble	_	
Mothanol	Incolublo		
Chycols	Insoluble	—	
Ethylene glycol	Swollen	_	
Glycerin	Swollen	Partially	
diyeerin	Swonen	soluble	
Propylene glycol	Swollen	Partially	
	bironen	soluble	
Acids		boluble	
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	1	1	
Isopropyl Ether	Insoluble	—	
Ethyl Ether	Insoluble	—	
1,4-Dioxane	Insoluble	—	
Methyl Cellosolve	Insoluble	—	
Cellosolve	Insoluble	Insoluble	
Hydrocarbons	Ter e a la della	1	
Ayiene	Insoluble	_	
Demzene	Insoluble		
Kerosene	Insoluble		
Chlorinated Hydrocarhons	monuble		
Chlorohenzene	Insoluble		
Carbon Tetrachloride	Insoluble	_	
Trichloroethvlene	Insoluble		
Ethylene Dichloride	Insoluble	_	
Methylene Chloride	Insoluble	_	
Aldehydes			
Butyraldehyde	Partially	_	
	soluble	—	
Formalin	soluble		
Ketones	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]

Туре	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 celluloseproducts (USP specifications)

Properties	Description	
Physical appearance	White to almost white,	
	odorless, hygroscopic	
	granular powder or fine fibres.	
Bulk Density, g/cm <sup>3</sup>	0.52 g/cm <sup>3</sup>	
Tapped density, g/cm <sup>3</sup>	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%	5–13 000 mPa s	
w/v aqueous solution		

#### 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.

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

Table 18: Applications of me	ethyl and ethyl cellulose [8	3,12]	
11		· .	

**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	METHOCEL Product
	Ingredient	
1	High-dose, low-	A15 Premium LV; E5 Premium
	solubility drug	LV
2	High-dose, high-	E5 Premium LV; K3 Premium
	solubility drug	LV
3	Low-dose, low-	A15 Premium LV; K3 Premium
	solubility drug	LV; E5 Premium LV
4	High-dose, high-	A15 Premium LV; K3 Premium
	solubility drug	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 eves. HPC is used as a sieving matrix for DNA separations capillary and microchip by electrophoresis.

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

Encapsulation	Micro and macro	Soluble, edible,
	encapsulation	flexible film
		barrier, fast
		release
Extrusion	Film and sheet	Thermoplastic,
	profiles and	binder, water and
	filaments	solvent soluble
Molding	Injection,	Thermoplastic,
	compression and	binder, water and
	blow molding	solvent soluble
Pharmaceuticals	Tablet binder,	Aqueous and
	tablet coating,	solvent solubility,
	modified release	thermoplastic
	liquids and semi	binder, non-ionic,
	solids.	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	Thickening and		
	paint	protective colloid,		
		Water-binding		
Cosmetics	Hair conditioners	Thickening and		
	Toothpaste Liquid	stabilizing		
	soaps and bubble bath			
	Hand creams and			
	lotions			
Adhesives	Wallpaper adhesives	Thickening,		
	Latex adhesives	lubricity, water-		
	Plywood adhesives	binding and solids		
		holdout		
Pharmaceuticals	Lotions and emulsions	Thickening,		
	Jellies and ointments	stabilizing and		
		water-binding		
	Ophthalmic and topical	Thickening agent		
	formulations			
	Tablets	Binder and film		
		coating agent		
Polymerization	PVAC and acrylic	Protective colloid		
	latices PVC suspension	and surface activity		
Industry	Paper, Textiles,	Adhesives,		
	Laundry Aids,	decorative and		
	Binders	protective coatings,		
		emulsion		
		polymerization		
Miscellaneous	Joint cements	Thickening, water-		
	Hydraulic cements	binding, set		
	Plaster	retarder, rheology		
	Caulking compound	control, stabilizing,		
	and putty	protective coating		
	Printing inks	and polymerization		
	Asphalt emulsions			

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

#### Conclusion

The drug development business has become truly global, especially in the area of procurement of components, manufacture, outsourcing of 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.

#### Acknowledgement

One of the authors thanks AICTE, New Delhi for granting fellowship during my course.

#### **Conflict of Interest**

The authors report no conflicts of interest.

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