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,

Key words

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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).

\[
\text{ROH} + R'\text{Cl} \rightarrow \text{RO}R' + \text{HCl}
\]

Equation 1: Etherification of cellulose. R= organic radical (CH₃-, C₂H₅–, 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 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 |

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.
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].

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 | ●                | ●               | ●          | ●   | ●   | ●                | ●              |

Nomenclature:
An example [10]-
HPMC E 15 premium LV
Low viscosity
For pharmaceutical use
Viscosity (15 mPa.s for a 2% solution in water at 20°C)
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 FAMC: hydroxypropyl methylcellulose 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 Type | Chemica l type | Available viscosities , cps | Meth oxyl % | Hydr oxypr opyl % | Avg particle size (µm) |
|--------------|----------------|-----------------------------|-------------|------------------|------------------------|
| Methocel A premium | Methyl cellulose USP | 15, 400, 1,500, 4,000 | 27.5-31.5 | 0 | 95.6 |
| 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- | 4.75 | 65 |
| Methocel J premium | Hypromellose 2906 | 19- | 4-12 | 64.7 |
| Methocel K premium | Hypromellose 2208 | 3, 4,000, 15,000, 100,000 | 19- | 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 H₂O 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 degree ofsolubility |
|---------|------------------|-------------------------------|
| 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 |
| Glycerol | 127 | 100 | Completely soluble |
| Monoacetate | | | |
| Glycerol 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.

![Chemical structure of ethyl cellulose](Image)

**Figure 4: Chemical structure of ethyl cellulose**

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

- Identifies physical form (fine particle)
- Identifies product grade (premium or industrial grade)
- Indicates viscosity
- Identifies ethoxyl type, content (Std., Med)

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 80% toluene and 20% ethanol. For all other ethyl cellulose products, solvent is 60% toluene and 40% ethanol. For a 5% solution is measured at 25°C. For medium products the viscosity of that product in milli Pas. For all other ethyl cellulose products, solvent is 60% toluene and 40% ethanol. For all other ethyl cellulose products, solvent is 60% toluene and 40% ethanol. For all other ethyl cellulose products, solvent is 60% toluene and 40% 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 mP as 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) |
| 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 9-11 | 48.0-49.5% | 375.0 |
| ETHOCEL Std 10 premium | 9-11 | 48.0-49.5% | |
| ETHOCEL Std 10FP premium | 9-11 | 48.0-49.5% | 3.0-15.0 |
| ETHOCEL Std 12.6-14 premium | 12.6-15.4 | 48.0-49.5% |  |
| ETHOCEL Std 10 premium | 18-22 | 48.0-49.5% |  |
| ETHOCEL Std 41-49 | 48.0-49.5% |  |
| ETHOCEL Med 45-55 | 45.0-46.5% | |
| ETHOCEL Med 63-77 | 45.0-46.5% | |
| ETHOCEL Std 90-110 | 48.0-49.5% | 45.0-46.5% | 465.0 |
| ETHOCEL Std 100 premium | 90-110 |  |
| ETHOCELStd 180-200 premium | 180-220 | 48.0-49.5% |  |
| ETHOCEL Std 270-300 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                         | Alcohols | Ketones | Acetates | Esters of hydroxy acids | Acids | Amines | Ethers | Polyhydric alcohols | Ketones  | Polyhydric alcohols | Ketones  | Polyhydric alcohols | Ketones  | Polyhydric alcohols | Ketones  |
|--------------------------------|----------|---------|----------|-------------------------|-------|--------|--------|---------------------|----------|---------------------|----------|---------------------|----------|---------------------|----------|
| A. HYDROCARBONS                |          |         |          |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
| Type                           | Name of solvent | Solubility |         |                          |       |        |        |                     |          |                     |          |                     |          |                     |          |
| 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  |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
| Cycloaliphatic hydrocarbons    | Cyclo hexane, methyl cyclohexane | Swells | Insol   |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
|                                | Cyclohexane    | 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         | Methanol, anhydrous, isobutanol, butanol | Sol clear; swells | Sol gels |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
|                                | Ethanol, sec-butanol, octyl(2-ethylhexyl) alcohol | Sol clear; swells | Gels    |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
|                                | Isopropanol    | Sol clear; swells | Swells  |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
|                                | Cycohexanol    | Gels | Sol clear |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
|                                | Furfuryl alcohol, tetrahydrofurfuryl alcohol, methyl cyclohexanol | Sol clear | Gels    |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |
|                                | Benzyl alcohol, phenyl ethyl alcohol | Sol clear | Sol clear |                         |       |        |        |                     |          |                     |          |                     |          |                     |          |

**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 -OCH₂CH(OH)CH₃ 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].

**Table 11: Hydroxypropyl cellulose product grades**

**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                 |
| JF              | 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 |
|-----------------|------------------------------------|--------|
| H CS, HF pharm  | 1,500-3000                         | 1,150,000 |
| M CS, MF pharm  | 4,000-6,500                        | 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  | 75-150                             | 80,000  |

| Viscosity types | Concentration in anhydrous alcohol by weight, % | Mol wt |
|-----------------|------------------------------------------------|--------|
| H CS, HF pharm  | 1,000-4,000                                     | 1,150,000 |
| M CS, MF pharm  | 3,000-6,500                                     | 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 Brookfield 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<br>Min. 99% through 20 mesh<br>Industrial grade: Min. 80% through 20 mesh<br>Min. 98% through 20 mesh<br>Min. 80% through 100 mesh<br>Min. 90% through 80 mesh<br>Min. 99.9% through 60 mesh |
| Particle size: fine X-grind |                                                                               |
| Bulk Density, g/ml         | 0.5 (varies with type)                                                        |
| pH                        | Neutral to litmus (1% solution/water)                                         |
| Softening temperature     |                                                                               |
| Burn out temperature in N₂ or O₂ | 100-150°C<br>450-500°C                                                       |
| Max. moisture content, (as packed)% | 5.0                                                                          |
| Specific gravity, g/cc (2% solution at 30°C) | 1.010                                                                       |

Solubility:
Hydroxypropylcellulose 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°C and 45°C. This precipitation is completely reversible. The polymer redissolves upon cooling the system below 40°C with stirring and the original is restored. When the temperature reaches 40 to 45°C, this precipitation is evidenced by appearance of cloudiness in the solution and reduction in viscosity.

List of solvents for Hydroxypropyl cellulose [25]:

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

- MODERATELY GRANULAR AND/OR HAZY
  - Acetone: Methyl acrate
  - Butyl acetate: Methyl ethyl ketone
  - Butyl cellosolve: Methylene chloride
  - Cyclohexanone: Naphtha:ethanol (1:1)
  - Isopropyl alcohol 99%: Tertiary butanol
  - Lactic acid: Xylene: isopropyl alcohol (1:3)

- INSOLUBLE
  - Aliphatic hydrocarbons: Mineral oils
  - Benzene: Soybean 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](Image)

**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, mPas\s |
|----------------------|-------------------------------------------------------|
| CELLOSIZE DCS LV (170 KB PDF) | 5000 (2% solution) |
| CELLOSIZE DCS HV (170 KB PDF) | 50000 (2% solution) |

| CELLOSIZE EP Grades | Viscosity Range of Aqueous Solution, LVF Brookfield at 25°C, mPas\s |
|---------------------|---------------------------------------------------------------|
| CELLOSIZE EP 09 hydroxyethyl cellulose | 90-160 (5% solution) |
| CELLOSIZE EP 300 hydroxyethyl cellulose | 250-400 (2% solution) |

| CELLOSIZE ER Grades | Viscosity Range of Aqueous Solution, LVF Brookfield at 25°C, mPas\s |
|---------------------|---------------------------------------------------------------|
| 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 | Viscosity Range of Aqueous Solution, LVF Brookfield at 25°C, mPas\s |
|---------------------|---------------------------------------------------------------|
| 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 | Viscosity Range of Aqueous Solution, LVF Brookfield at 25°C, mPas\s |
|------------------------|---------------------------------------------------------------|
| CELLOSIZE HMHEC 500 hydrophobe - modified hydroxyethyl cellulose | 113-150 (5% solution) |
| CELLOSIZE QP Grades | Viscosity Range of Aqueous Solution, LVF Brookfield at 25°C, mPas\s |
|---------------------|---------------------------------------------------------------|
| CELLOSIZE QP 09H hydroxyethyl cellulose | 113-150 (5% solution) |
| CELLOSIZE QP 09L hydroxyethyl cellulose | 75-112 (5% solution) |
| CELLOSIZE QP 10000H hydroxyethyl cellulose | 1100-1500 (1% solution) |
| CELLOSIZE QP 15000H hydroxyethyl cellulose | 4400-6000 (1% solution) |
| CELLOSIZE QP 20000 hydroxyethyl cellulose | 215-282 (5% solution) |
| CELLOSIZE QP 3L hydroxyethyl cellulose | 300-400 (2% solution) |
| CELLOSIZE QP 5L 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) |
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**

| Product               | Description                                      |
|-----------------------|--------------------------------------------------|
| CELLOSIZE HEC-10       | 4400-6500 (1% solution)                          |
| CELLOSIZE HEC-15       | 50-80 (2% solution)                              |
| CELLOSIZE HEC-18       | 250-400 (2% solution)                            |
| CELLOSIZE HEC-25       | 4400-6500 (1% solution)                          |
| CELLOSIZE HEC-60       | 180-325 (2% solution)                            |
| CELLOSIZE HEC-10 HV    | >6000 (1% solution)                              |
| CELLOSIZE HEC-25 HV    | >6000 (1% solution)                              |

**HEC Products for Personal Care Applications**

| Product               | Description                                      |
|-----------------------|--------------------------------------------------|
| CELLOSIZE Polymer PCG-10 | 4400-6000 (1% solution)                        |
| CELLOSIZE QP 40        | 80-125 (2% solution)                             |
| CELLOSIZE QP 300       | 300-400 (2% solution)                            |
| CELLOSIZE QP 4400H     | 4800-6000 (2% solution)                          |
| CELLOSIZE QP 15000H    | 1100-1500 (1% solution)                          |
| CELLOSIZE QP 30000H    | 1500-2400 (1% solution)                          |
| CELLOSIZE QP 52000H    | 2400-3000 (1% solution)                          |
| CELLOSIZE QP 100MH     | 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**     | 0.3-0.6                                           |
| **Apparent density, g/ml**  | 0.35-0.61                                         |
| **pH**                      | 6.0-8.5                                           |
| **Softening Point, °F (°C)**| >285 (140)                                        |
| **Decomposition Temperature, °F (°C)**| About 400 (205)                                    |
| **Viscosity (mPa.s), 20°C aqueous solution**| 5-60000                                         |
| **Specific Gravity at 20/20°C**| 1.30-1.40                                      |

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    |             |
| 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  | —           |
| Methyl salicylate         | Insoluble  | —           |
| **Ethers**                |           |             |
| Isopropyl Ether           | Insoluble  | —           |
| Ethyl Ether               | Insoluble  | —           |
| 1,4-Dioxane               | Insoluble  | —           |
| Methyl Cellosolve         | Insoluble  | —           |
| Cellosolve                | 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                  | Insoluble  | —           |
| **Ketones**               |           |             |
| Acetone                   | Insoluble  | —           |
| Diethyl Ketone            | Insoluble  | —           |

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.
E. Carboxymethyl cellulose:

Carboxymethyl cellulose (CMC) or cellulose gum is a cellulose derivative with carboxymethyl groups (-CH₂-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.

![Chemical structure of Carboxymethyl cellulose](image)

**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 replacement. In the food industry, there are "7", "9", and "12" 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 indicate a "regular" particle size.
- 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 "H" signifies a high viscosity grade, there are "L", "M", and "H" types, representing low, medium, and high viscosity respectively.

| 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 16: Carboxymethyl cellulose product grades [30,31]**

| Properties       | Description                               |
|------------------|-------------------------------------------|
| Physical appearance | White to almost white, odorless, hygroscopic granular powder or fine fibres. |
| Bulk Density, g/cm³ | 0.52 g/cm³ |
| Tapped density, 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.

| Amines          | Soluble  | —  |
|-----------------|----------|---|
| Ethylendiamine  | 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 | —  |
| Phenol          | Soluble  | Insoluble |
| Aniline         | Soluble  | —  |
| Ethylene chlorohydrin | Soluble | —  |

**Table 17: Description of Carboxymethyl cellulose products (USP specifications)**
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 compatibility 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 E5 LV, E15 LV, A15 LV, 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, K4M, 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 |

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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, Textile 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 | PVC 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 |

**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.

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