Hydroxypropyl Methylcellulose (HPMC): As A Multitasking Excipient

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***Abstract*-There are numerous applications for hydroxypropyl methylcellulose (HPMC) in food and pharmaceutical formulations. Applications for it include coating polymers, bio adhesives, viscolizing agents (thickening agents), binder in granulation processes, solid dispersion to improve solubility, and modified release formulations. been thoroughly recorded. Another noteworthy application is the creation of capsule shells, which substitute animal-derived gelatin for the traditional two-piece capsule's gelatin.This review's objective is to comprehensively examine the basic history, types, physicochemical properties, different methods of synthesis, uses, handling precautions, storage conditions, different in compatibilities, adverse effect, different evaluation like Assay, pH, UV, IR, etc., information about patents and its expiry these all points are covered in this review**

General Description -

HPMC (hydroxypropyl methyl cellulose) is partly methylated and o-(2-hydrxypropylated) cellulose obtained by reacting alkali cellulose with propylene oxide and chloromethane. It is also known by various synonyms i.e., Hypromellose, methocel, Benecel MHPC, methylcellulose propylene glycol ether, methyl hydroxypropyl cellulose, Metolose, and Tylopur . Its empirical formula is C8H15O8 -(C10H18O6) n -C8H15O8 (Fig. 1). It is white/ creamy white, tasteless, odorless, fibrous or granular powder and is soluble in cold water Its solutions are stable at pH 3-11 and its viscosity increases upon increasing temperature. Upon heating and cooling, it undergoes a reversible sol-gel transformation. Relying upon the concentration and grade of HPMC, its gel point is 50-90°C. On long term storage, its aqueous solutions have good viscosity and are enzyme resistant. Its aqueous solutions are prone to microbial attack, so an anti-microbial preservative is required to be added. For example, HPMC, when used as viscosity increasing agent in ophthalmic solutions, is used with benzalkonium chloride as preservative. Its aqueous solutions are sterilized by autoclave and redispersed upon cooling by shaking. HPMC powder is stored in a cool and dry place in a well closed container Aqueous dispersions of HPMC are prepared by dispersing it in 25% hot water maintained at 80°C followed by the addition of cold water with stirring. Its gels are stable at pH 1-3. Viscosity of HPMC dispersions depends on molecular weight of polymer grade, presence of additives and vehicle composition. [1]. HPMC is a water soluble nonionic cellulosic polymer in which some of the hydroxyl groups are substituted with methoxy and hydroxypropyl groups as a binder, HPMC is used at the concentration of 2%–5% w/w, however, it has been commonly used as tablet film coating polymer. The polymer chain length, size and degree of branching determine the viscosity of the polymer in solution. In general, a tablet film coating requires low viscosity polymers. Using low viscosity polymers, the solid content in the coating. [2]

Discovery & Future History

Hydroxypropyl Methylcellulose (HPMC) is a cellulose derivative that is widely used in the pharmaceutical, food, and cosmetic industries. The discovery and development of HPMC have significantly contributed to the improvement of various applications. Here's an overview of the discovery and future history of HPMC:

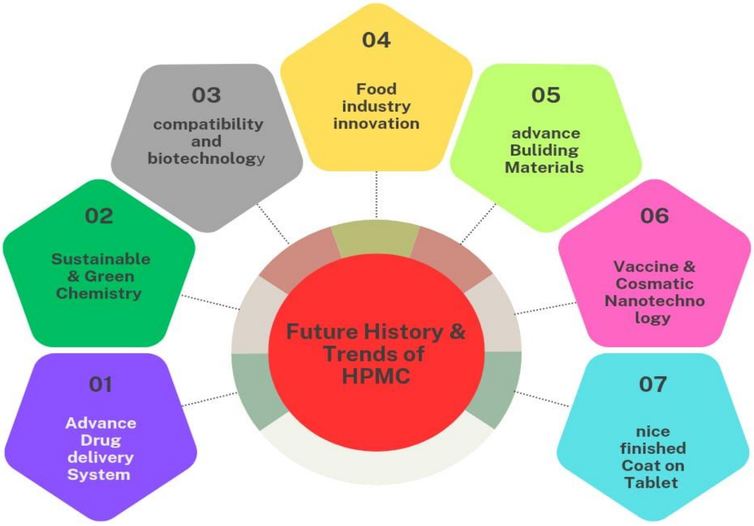
Discovery of HPMC

- Origin of Cellulose: The history of HPMC begins with the discovery of cellulose in 1838 by French chemist Anselme Payen. Cellulose is the primary structural component of plant cell walls, and its ability to form gels, films, and fibers made it an important material in industries [37].
- Modification of Cellulose: The process of modifying cellulose to create different derivatives like methylcellulose, hydroxyethylcellulose, and HPMC began in the early 20th century. Researchers found ways to alter the properties of cellulose to make it more versatile. In the case of HPMC, the main modification involves adding

hydroxypropyl and methyl groups to cellulose.[38]

- Commercial Development: HPMC was first developed and commercialized in the mid-20th century. It emerged as a product with unique properties such as water solubility, gel formation, film-forming abilities, and being biocompatible, making it especially useful in a wide range of applications. [39]

Future History and Trends



- Advancements in Drug Delivery Systems: As the pharmaceutical industry evolves, there is an increasing demand for more sophisticated drug delivery systems. HPMC will play a key role in the development of controlled-release formulations and personalized medicine. Research into biodegradable HPMC-based drug delivery systems could revolutionize treatments for chronic diseases.
- Sustainable and Green Chemistry: With growing concerns about sustainability, there is an increasing focus on producing HPMC from renewable sources and reducing the environmental impact of its production. Innovations in green chemistry may allow for more eco-friendly processes to produce HPMC and its derivatives.
- Biocompatibility and Biotechnology: The medical and biotechnology industries will continue to find new uses for HPMC in areas such as tissue engineering, wound healing, and drug delivery. Its biocompatibility, biodegradability, and ability to form hydrogels are expected to lead to new applications in regenerative medicine. [40]
- Food Industry Innovation: The food industry will continue to explore HPMC as a plant-based alternative to animal-derived ingredients like gelatin and as a solution to meet the demands of a growing vegan and vegetarian population.
- Advanced Building Materials: The construction industry is likely to see further innovations in the use of HPMC, especially in the development of more sustainable and energy-efficient building materials.
- Nanotechnology: As nanotechnology continues to develop, HPMC may be used in the formulation of nanoparticles for drug delivery, vaccines, and cosmetic applications.

Synonyms-

Hydroxypropyl Methylcellulose (HPMC) is known by several synonyms or alternative names, depending on the industry and context. Here are some common synonyms: [3]

1. Hypromellose – This is the most widely used synonym, especially in the pharmaceutical industry. [4]
2. Cellulose, hydroxypropyl methyl ether – A technical name based on its chemical structure.
3. Methocel – A trademarked name for HPMC products by Dow Chemical.
4. E464 – The food additive code for HPMC under the European Union's classification system.

5. Modified Cellulose – A general term used for cellulose derivatives like HPMC.
6. HPMC Phthalate – A derivative of HPMC used in enteric coatings.
7. Hydroxypropyl Methyl Ether of Cellulose – A descriptive chemical name.
8. Hypromellosum – Another variation used in certain pharmacopeias.
9. Hydroxypropyl Methylenecellulose – Another technical variation of the chemical name.
10. Methoxypropyl Cellulose – A less common synonym highlighting its methoxypropyl groups.
11. Pharmacoat – A brand name for HPMC in pharmaceutical applications.
12. Benecel – Another trademarked name for HPMC products, often used in industrial contexts.
13. Cellulose Ether – A broad category name sometimes used interchangeably.
14. Viscosity Modifier – Although more of a functional descriptor, it is sometimes referred to this way in industrial uses.
15. Methylhydroxypropylcellulose – An alternate technical descriptor of HPMC

Types of HPMC

HPMC can be classified based on its grade, application, or specific properties. Here are some common types:

Pharmaceutical Grade HPMC:

Used as a binder, film-former, and controlled-release agent in tablet formulations.Includes subcategories like low-viscosity, medium-viscosity, and high-viscosity grades depending on the desired application.

Food Grade HPMC:

Approved as a food additive (E464) for use as a thickener, emulsifier, or stabilizer in processed foods.Often used in vegan and vegetarian products as a gelatin replacement.

Industrial Grade HPMC:

Primarily used in construction applications like cement, mortar, tile adhesives, and wall putty for water retention and improved workability.

Cosmetic Grade HPMC:

Used in personal care products such as creams, lotions, and shampoos for its thickening and stabilizing properties.

HPMC for Enteric Coating:

Specially modified forms like HPMC phthalate are used for protecting active ingredients in pharmaceuticals by providing an enteric coating. [4]

Low-Substituted HPMC (L-HPMC):

A type of HPMC with reduced substitution levels, often used in disintegrants for rapid tablet dissolution.

Specialized HPMC Blends:

Customized blends designed for specific applications, such as thermal gelation or sustained drug release.

Types on basic of Medical grades

HPMC is generally classified into three grades HPMC is generally classified into three grades: K, E, and F, which represent different degrees of substitution for methoxy and hydroxypropyl groups. [5]

Table.1 - some common medical-grade HPMCs

Grades	Viscosity Grades	Main Applications and Properties
HPMC K4M	4000	HPMC is often used in medicines as a base for slow-release formulations. It helps control the release of the active ingredient over a longer period
HPMC K15M	15000	It’s commonly used to bind tablets, create controlled-release drugs, and thicken liquid medicines
HPMC K100M	100000	

		HPMC provides strong thickening and gelling properties, making it useful in slow-release medications and as an adhesive in tablet production.

Physicochemical properties

Table .2 . Physicochemical properties

Property	Details
Structure	Derived from cellulose, consisting of repeating β-(1→4)-linked D-glucose units modified with methoxy and hydroxypropyl groups. [6]
Chemical Name	Cellulose, 2-hydroxypropyl methyl ether
IUPAC Name	(2-Hydroxypropyl)methyl ether of cellulose
Molecular Formula	Variable, depending on the degree of substitution; general formula: [C6H7O2(OH)3−x−y(OCH3)x(OCH2CH(CH3)OH)y]n[C_6H_7O_2(OH)_3-x-y(OCH_3)_x(OCH_2CH(CH_3)OH)_y]_n
Molecular Weight	Variable, depending on chain length and substitution; typical molecular weights range between 10,000 and 1,500,000 Da.
Solubility	Soluble in cold water, forming clear viscous solutions; insoluble in hot water; slightly soluble in ethanol-water and acetone-water mixtures. [7]
Melting Point	HPMC does not have a sharp melting point but undergoes thermal decomposition at temperatures above 200–250 °C.
Density	1.26 g/cm³ (bulk density varies depending on the grade and particle size).
Taste	Tasteless
Appearance	White to off-white powder or granules
pH	pH Stable in the pH range of 3–11
Viscosity	Viscosity varies depending on grade and concentration; ranges from 5 mPa·s to over 200,000 mPa·s in a 2% aqueous solution at 20 °C
Moisture Content	Typically, ≤5% (hygroscopic).
Optical Rotation	Optically inactive due to the absence of chiral centers in modified cellulose molecules
Thermal Gelation	Exhibits thermally reversible gelation; gelation temperature depends on the substitution level and concentration (typically 50–90 °C).
Surface Activity	Exhibits emulsifying and stabilizing properties
Compatibility	Compatible with many other hydrophilic polymers, electrolytes, and additives used in pharmaceutical and food applications. [8]

Method of Synthesis-

The synthesis of Hydroxypropyl Methylcellulose (HPMC) involves the following steps:

1.Cellulose Preparation

Purified cellulose (usually from wood pulp or cotton) is used as the raw material.

2. Alkalization

The cellulose is treated with a solution of sodium hydroxide (NaOH), making it alkaline and reactive. This step produces alkali cellulose. [8]

3. Etherification

The alkali cellulose reacts with methyl chloride ($CH_3 Cl$) to introduce methoxyl ($-OCH_3$) groups.Simultaneously, it reacts with propylene oxide ($C_3 H_6 O$) to introduce hydroxypropoxyl ($-OCH_2 CH(OH)CH_3$) groups.dual reaction leads to the formation of HPMC with specific degrees of substitution (methoxy and hydroxypropyl groups). [9]

4. Neutralization and Purification

- The reaction mixture is neutralized with acid to remove residual alkali. The product is washed to remove salts and impurities. [10]

5. Drying and Milling

- The purified HPMC is dried and ground into a fine powder.

Applications

- 1. Pharmaceutical Applications
- HPMC is widely used in drug formulations due to its biocompatibility, safety, and versatility.[11]

Table.3 pharmaceutical use

Function/Use	Details	Concentration Range
Thickener in Gels and Creams	Provides viscosity and stability in skincare formulations.	0.5–3%
Film-Forming Agent	Forms flexible, non-tacky films in hair sprays and styling gels.	0.5–2%
Emulsifier and Stabilizer	Stabilizes emulsions in creams and lotions.	0.2–1%
Binder in Toothpaste	Binds ingredients together and provides a smooth texture.	0.5–1%
Moisturizer	Retains water and prevents drying in cosmetic products.	0.1–0.5%

2. Food Industry

HPMC is an approved food additive (E464) with diverse applications.

Table 4. Food Industry

Function/Use	Details	Concentration Range
Thickener and Stabilizer	Used in sauces, soups, dressings, and desserts to control texture and viscosity.	0.25–1%
Emulsifier	Stabilizes oil-water emulsions in processed foods.	0.1–0.5%
Fat Replacer	Mimics the texture and mouthfeel of fats in low-fat food products.	0.5–2%
Foam Stabilizer	Stabilizes foams in beverages, whipped toppings, and desserts.	0.1–0.4%
Edible Films and Coatings	Acts as a protective coating for fruits, vegetables, or candies.	1–3%
Gluten-Free Baking	Improves dough elasticity, gas retention, and crumb structure in gluten-free baked goods.	0.5–2%
Moisture Retention	Prevents moisture loss in frozen foods or baked goods.	0.3–1%

3. Personal Care and Cosmetics

HPMC is commonly found in skin, hair, and oral care products due to its mild and non-irritating properties.

It is use as a thickener gels & Creams

Table .5 Personal Care and Cosmetics

Function/Use	Details	Concentration Range
Tablet Binder	Improves tablet strength and integrity during manufacturing.	2–5%
Film Coating Agent	Forms protective and aesthetic coatings; improves tablet stability and controlled release.	2–20%
Controlled/Sustained Release	Used in hydrophilic matrix tablets for extended drug release.	10–50%
Thickener and Gelling Agent	Enhances viscosity in oral liquids, suspensions, and gels.	0.5–5%
Capsule Shell Material	Used in vegan, plant-based capsule shells (alternative to gelatin).	Up to 100% (pure HPMC shells)
Mucoadhesive Agent	Improves adhesion of formulations like eye drops or buccal tablets.	0.5–2%
Stabilizer in Suspensions	Prevents settling and aggregation in liquid suspensions.	0.1–2%

Eye Drops (Artificial Tears)	Provides lubrication and relief for dry eye syndrome.	0.3–0.8%

4. Construction Industry

HPMC improves workability and performance in cement-based products.

Table .6. Construction Industry

Function/Use	Details	Concentration Range
Water Retention Agent	Retains moisture in cement and plaster to improve curing.	0.1–0.5%
Thickener and Binder	Enhances workability and adhesion of tile adhesives, mortars, and joint compounds.	0.1–0.3%
Lubricant	Improves application smoothness in construction materials.	0.1–0.5%
Anti-Sagging Agent	Prevents sagging in tile adhesives and wall plasters.	0.2–0.4%

5. Paints, Coatings, and Adhesives

HPMC is widely used in industrial applications to improve stability and performance.

Table .7. Paints, Coatings, and Adhesives

Function/Use	Details	Concentration Range
Thickener	Enhances viscosity and consistency in latex paints and coatings.	0.5–2%
Rheology Modifier	Provides shear-thinning properties for easy application.	0.1–0.5%
Binder	Improves adhesion and cohesion in adhesives.	0.5–2%

6. Miscellaneous Uses

HPMC has a wide range of additional applications: [12]

Table .8. Miscellaneous Uses

Function/Use	Details	Concentration Range
Printing Ink	Acts as a viscosity modifier and stabilizer in ink formulations.	0.5–2%
Detergents	Improves texture and stabilizes liquid detergents.	0.1–1%
Oil Well Drilling	Used as a viscosifier and fluid loss control agent in drilling muds.	0.5–1.5%

Handling precautions

1. Personal Protective Equipment (PPE):
   - Wear gloves, safety goggles, and protective clothing to avoid contact with skin and eyes.
2. Dust Control:
   - Minimize dust generation during handling.
   - Use dust extraction systems or local exhaust ventilation in dusty environments.
3. Inhalation Protection:
   - Avoid inhaling HPMC dust, as it may cause respiratory irritation.
   - Use a dust mask or respirator (e.g., N95) in areas with high dust concentration.
4. Skin and Eye Contact:
   - Avoid direct or prolonged contact with skin and eyes.
   - In case of contact, rinse thoroughly with water.
5. Hygiene Practices:
   - Wash hands thoroughly after handling and before eating, drinking, or smoking.
6. Moisture Sensitivity:
   - Store HPMC in a cool, dry, and well-ventilated area.
   - Keep containers tightly closed to prevent moisture absorption, as HPMC is hygroscopic.
7. Avoid Ignition Sources:
   - Keep away from open flames, sparks, or high heat, as fine HPMC dust may form explosive mixtures in air.
8. Spill Management:
   - Carefully sweep up spills to minimize dust.
   - Dispose of the material according to local environmental regulations.
9. Waste Disposal:
   - Avoid releasing HPMC into sewers or natural water bodies.
   - Follow local, state, and federal guidelines for disposal. [13]

Storage

storage and packaging conditions to maintain the stability of Hydroxypropyl Methylcellulose (HPMC):

1. Temperature:
    - Store HPMC in a cool environment, ideally below 25°C (77°F).
    - Avoid exposure to extreme heat, as it can degrade the material. [33]
2. Humidity Control:
    - Keep HPMC in a dry area with low humidity, as it is hygroscopic and can absorb moisture from the air.
    - Use a dehumidified storage area if necessary to prevent clumping or loss of functionality.
3. Packaging:
    - Store in tightly sealed containers made of moisture-resistant materials like polyethylene-lined drums or aluminum-coated bags.
    - Ensure the packaging is airtight to prevent contamination and moisture ingress. [34]
4. Light Protection:
    - Protect HPMC from direct sunlight and UV exposure, as prolonged light exposure can degrade its properties.
    - Use opaque or light-blocking packaging if possible.[35]
5. Avoid Contaminants:
    - Store away from chemicals, strong odors, or volatile materials to prevent cross-contamination or absorption of odors. [36]
6. Ventilation:
    - Keep the storage area well-ventilated to prevent condensation and maintain air circulation.
7. Handling in Storage:
    - Do not stack containers too high to avoid damage to the packaging.
    - Label and organize storage to ensure first-in-first-out (FIFO) inventory management. [14]

Incompatibilities

While HPMC is generally considered to be safe and non-reactive with most drugs, it can have some interactions with certain drugs and chemicals. Here are some potential incompatibilities and interactions to be aware of:

Effect on Drug Release

- HPMC is used in controlled-release formulations, and its interaction with drugs can affect the release profile. Some drugs may not release at the desired rate when mixed with HPMC.
- Example: Certain salts or basic drugs can interact with the polymer and alter its gelling properties, which might impact the drug's bioavailability or release.

2. Interaction with Electrolytes

- Electrolytes (e.g., sodium chloride): High concentrations of salts might affect the hydration properties of HPMC, potentially altering the gelation and dissolution characteristics of the formulation.
- Example: In high-salt environments, the swelling behavior of HPMC can be reduced, leading to poor drug release.[28]

3. Alkaline Solutions

- Alkaline conditions (pH above 8): HPMC can undergo changes in viscosity when exposed to highly alkaline conditions. This could influence the stability of both the excipient and the active pharmaceutical ingredient (API).
- Example: In formulations involving alkaline buffer solutions, HPMC might lose its thickening properties, altering the desired consistency of the product.[29]

4. Interactions with Certain Surfactants

- Surfactants: Some surfactants, especially anionic surfactants (e.g., sodium lauryl sulfate), can interact with HPMC and potentially reduce its effectiveness as a binder or film former.
- Example: In tablet formulations, excessive surfactant concentrations could interfere with the binding action of HPMC, leading to reduced tablet integrity.[30]

5. Water-soluble Drugs

- HPMC can interact with highly water-soluble drugs in a way that alters their dissolution rates. This may be desirable in controlled-release formulations but undesirable in immediate-release formulations.
- Example: Some water-soluble drugs might form poorly soluble complexes with HPMC, which could affect dissolution and bioavailability.

6. Acidic Solutions

- In acidic conditions (e.g., pH less than 4), HPMC can undergo some changes in its structure that may affect its viscosity and gelling properties, leading to unpredictable behavior in formulations.
- Example: Drugs that require an acidic pH for optimal solubility may experience altered dissolution characteristics when combined with HPMC in such environments. [31]

7. Polymeric Interactions

- Other cellulose derivatives: HPMC may interact with other cellulose derivatives (e.g., hydroxypropyl cellulose or methylcellulose), which could alter the overall performance of the formulation.
- Example: Mixing different cellulose-based polymers in a formulation may lead to phase separation or inconsistencies in release profiles. [8]

General Safety

Toxicity: HPMC is generally regarded as safe and non-toxic, with no known significant interactions in most drug formulations. However, very high concentrations may cause local irritation or gastrointestinal discomfort in some individuals.

Adverse effects

Hydroxypropyl Methylcellulose (HPMC) is generally regarded as a safe excipient with minimal adverse effects, especially in pharmaceutical formulations. However, when used over extended periods or in certain formulations, it could potentially lead to some specific long-term side effects, though these are rare. Here are some more specific adverse effects that have been reported with long-term or excessive use of HPMC:

1. Gastrointestinal Effects

- Bloating and Distention: In prolonged use, particularly in controlled-release formulations, HPMC’s gelling properties might cause bloating or abdominal distention. This is more likely in patients who have a sensitivity to polymeric excipients or those with gastrointestinal motility disorders.
- Example: HPMC’s hydrophilic nature allows it to absorb water, and in large amounts, it can lead to excessive swelling in the gastrointestinal tract, causing discomfort. [15]

2. Fiber-Like Effects

- Constipation or Diarrhea: Although HPMC is considered a non-absorbable fiber, in some cases, it may cause constipation or diarrhea if it binds excessively to water or disrupts normal bowel function. This is more common in individuals with preexisting gastrointestinal conditions, such as irritable bowel syndrome (IBS).
- Example: Overuse or poor hydration with HPMC-containing products may lead to constipation due to reduced intestinal motility. On the other hand, excessive water absorption may cause diarrhea.

3. Potential for Systemic Absorption (in very rare cases)

- Very High Doses: In exceptionally high doses, there is a theoretical risk of HPMC being absorbed into the systemic circulation, although this is extremely rare and unlikely to occur with typical pharmaceutical formulations. If absorbed in large quantities, it could potentially contribute to systemic effects, although no significant toxicity has been reported.
- Example: Prolonged high-dose topical use or consumption of HPMC-laden products may lead to systemic exposure, but this is considered highly unlikely and rare in pharmaceutical use.

4. Inhalation Toxicity (when used in dust form)

- Respiratory Issues: Prolonged exposure to HPMC dust, particularly during manufacturing processes, may lead to respiratory issues such as coughing, wheezing, or even chronic lung irritation. This risk is mainly associated with occupational exposure in pharmaceutical or manufacturing environments, rather than oral consumption of the excipient.
- Example: Chronic inhalation exposure in industrial settings may lead to symptoms of

pulmonary irritation or allergic reactions over time. [26]

5. Allergic Reactions

- Hypersensitivity Reactions: Although very rare, some individuals may experience hypersensitivity reactions to HPMC, manifesting as skin rashes, itching, or more severe reactions like anaphylaxis, especially if HPMC is used in topical formulations.
- Example: Topical products containing HPMC may cause localized irritation or allergic dermatitis in sensitive individuals after prolonged use. [27]

6. Interaction with Gut Flora

Changes in Gut Microbiota: There is some evidence suggesting that long-term consumption of cellulose-based excipients, including HPMC, might affect the composition of gut microbiota. The impact of such changes on overall gastrointestinal health and immunity is still not fully understood, but this could potentially alter digestion or immune responses in rare cases.

- Example: Chronic use of HPMC in high doses could potentially modify the balance of beneficial gut bacteria, leading to gastrointestinal discomfort or changes in nutrient absorption.

7. Impact on Drug Absorption

- Altered Drug Bioavailability: Long-term use of HPMC in formulations may alter the absorption profile of certain drugs, particularly those requiring fast absorption. HPMC’s gel-forming ability may slow down the dissolution rate of some drugs, leading to reduced bioavailability over time.
- Example: Chronic use of controlled-release formulations containing HPMC may result in slower absorption and altered plasma concentrations of drugs that are highly sensitive to changes in release rates. [16]

Evaluation

Hydroxypropyl methylcellulose (HPMC) is a versatile polymer extensively utilized in pharmaceutical formulations. Its quality and performance are evaluated through various analytical parameters, including assay, pH, loss on drying, and spectroscopic analyses such as UV and IR. Below is a detailed overview of these evaluation methods, along with their typical acceptance criteria and relevant references:

1. Assay:

The assay of HPMC quantifies its content within a formulation. A validated High-Performance Liquid Chromatography with Refractive Index Detection (HPLC-RID) method has been developed for this purpose. This method effectively separates HPMC from other components, ensuring accurate quantification. In tested samples, HPMC content ranged from 85% to 107% of the labeled amount, indicating the method's reliability. [17]

2. pH Measurement:

The pH of a 1% w/v HPMC solution is typically measured to ensure it falls within an acceptable range, usually between 5.5 and 8.0. The procedure involves dissolving HPMC in carbon dioxide-free water,[18] measuring the pH at 25°C ± 2°C using a calibrated pH meter.

3. Loss on Drying (LOD):

LOD assesses the amount of water and volatile substances present in HPMC. The standard method involves drying a known weight of the sample at a specified temperature (commonly 105°C) until a constant weight is achieved. The weight loss is then calculated as a percentage of the original sample weight. This parameter ensures the material's stability and suitability for use. [19]

4. Spectroscopic Analyses:

- UV Spectroscopy: UV imaging can be utilized to study the behavior of HPMC in solution. Baldursdottir et al. investigated the swelling, gelling, and erosion of HPMC in buffer solutions using UV imaging, providing insights into its performance in gastrointestinal conditions.
- IR Spectroscopy: Infrared (IR) spectroscopy is employed to confirm the chemical structure of HPMC by identifying characteristic functional groups. Specific absorption bands corresponding

to methoxy and hydroxypropyl groups can be observed, verifying the presence of these substituents in the polymer. [20]

Marketed products

Hydroxypropyl Methylcellulose (HPMC) is a versatile excipient utilized in various industries, including pharmaceuticals, food, and cosmetics. Below is a table listing some of the prominent brand names of HPMC, along with their respective manufacturers:

9.Brand name and manufacturer Table

Brand Name	Manufacturer
Methocel™	Dow Chemical Company
Benecel™	Shin-Etsu Chemical Co., Ltd.
Aqualon™	Ashland Global Holdings Inc.
Opadry™	Colorcon Inc.
Blanose™	Ashland Global Holdings Inc.

Hydroxypropyl Methylcellulose (HPMC) is a widely used excipient in various industries, including pharmaceuticals, cosmetics, and construction. Several brand names have been established for HPMC products. While specific research papers focusing solely on HPMC brand names are limited, the following references provide insights into the applications and properties of HPMC: [21]

1. Dow Chemical Company. "Methocel™ Cellulose Ethers Technical Handbook." Dow Chemical Company, 2002.

This technical handbook offers comprehensive information on Methocel™, a brand of HPMC produced by Dow Chemical Company, detailing its properties and applications.

2. Shin-Etsu Chemical Co., Ltd. "Pharmaceutical Excipients: Metolose®." Shin-Etsu Chemical Co., Ltd., 2010.

This publication provides detailed information on Metolose®, an HPMC product line from Shin-Etsu Chemical Co., Ltd., focusing on its use in pharmaceutical applications.

3. Ashland Global Holdings Inc. "Benecel™ and Aqualon™ Cellulose Ethers for Personal Care Applications." Ashland Global Holdings Inc., 2015.

This document discusses the properties and applications of Benecel™ and Aqualon™, HPMC brands offered by Ashland, in personal care products.

Patents

Hydroxypropyl Methylcellulose (HPMC) has been the subject of various patents focusing on its production methods, applications, and properties. Below is a selection of notable patents related to HPMC:

1. EP2078042A1 - Hydroxypropyl Methyl Cellulose Hard Capsules
   - Inventors: Not specified
   - Description: This patent describes a process for manufacturing HPMC hard capsules using a dip coating method. The process involves providing an aqueous composition of HPMC with specific methoxy and hydroxypropoxy content and viscosity parameters.
   - Year of Grant: 2009
   - Year of Expiry: 2029 [22]
2. CN103834042A - Preparation Method of Hydroxypropyl Methylcellulose Solution
   - Inventors: Not specified
   - Description: This invention discloses a method for preparing an HPMC solution by first mixing HPMC with hot water to form a mixture, then adding cold water, and stirring in an ice-water bath until a clear, viscous solution is obtained. [35]
   - Year of Grant: 2014
   - Year of Expiry: 2034
3. CN104558207A - Production Process of Hydroxypropyl Methyl Cellulose
   - Inventors: Not specified
   - Description: This patent outlines a production process for HPMC involving steps such as alkalization of purified cotton, etherification with chloromethane and epoxypropane, followed by neutralization, centrifugation, drying, and crushing to obtain the final product.
   - Year of Grant: 2015
   - Year of Expiry: 2035
4. US4614545A - Hydroxypropyl Methyl Cellulose Thickening Agents for Organic Liquids
   - Inventors: Not specified

  - Description: This patent discusses the use of HPMC ethers as thickening agents for organic liquids and their mixtures with water. It highlights the production methods and applications of these HPMC ethers in various industries. [23]
  - Year of Grant: 1986
  - Year of Expiry: 2006
5. CN106146674A - Hydroxypropyl Methyl Cellulose and Its Production and Use
  - Inventors: Not specified
  - Description: This invention discloses a type of HPMC with high solubility and product homogeneity, achieved through a specific production method involving etherification of methylcellulose with epoxy chloropropane. [36]
  - Year of Grant: 2016
  - Year of Expiry: 2036
6. EP3378874A1 - Method for Producing Hydroxypropyl Methyl Cellulose
  - Inventors: Not specified
  - Description: This patent provides a method for producing HPMC with high hydroxypropoxy content, low ash content, and low insoluble fiber content. The process includes steps such as contacting pulp with an alkali metal hydroxide solution, reacting with an etherifying agent, and subsequent purification steps. [37]
  - Year of Grant: 2018
  - Year of Expiry: 2038
7. US3839319A - Hydroxypropyl Methylcellulose Ethers and Method of Preparation
  - Inventors: Not specified
  - Description: This patent describes a process for preparing HPMC ethers soluble in cold water and anhydrous methanol. The method involves reacting alkali cellulose with a mixture of propylene oxide and methyl chloride under specific conditions.
  - Year of Grant: 1974
  - Year of Expiry: 1994
8. CN102807624A - Preparation Technology of Hydroxypropyl Methylcellulose Ether
  - Inventors: Not specified
  - Description: This invention relates to a preparation technology of HPMC ether, involving independent alkalization and a two-step etherification process to achieve the desired product characteristics.
  - Year of Grant: 2012
  - Year of Expiry: 2032
9. US20140088202A1 - Hydroxypropyl Methyl Cellulose Hard Capsules
10. Inventors: Not specified
  - Description: This patent discusses HPMC hard capsule shells containing HPMC with specific methoxy and hydroxypropoxy content and viscosity parameters, suitable for pharmaceutical applications.
  - Year of Grant: 2014
  - Year of Expiry: 2034
11. US11136415B2 - Method for Producing Hydroxypropyl Methyl Cellulose
  - Inventors: Not specified
  - Description: This patent provides a method for producing HPMC with high hydroxypropoxy content, low ash content, and low insoluble fiber content, involving steps such as contacting pulp with an alkali metal hydroxide solution, reacting with an etherifying agent, and subsequent purification steps. [24]
  - Year of Grant: 2021
  - Year of Expiry: 2041

CONCLUSION

Hydroxypropyl Methylcellulose (HPMC), also known as hypromellose, is a non-ionic, water-soluble cellulose ether derived from natural cellulose. It is extensively utilized in the pharmaceutical industry as an excipient due to its versatile properties, including film-forming, thickening, and controlled-release capabilities. HPMC is employed in various dosage forms such as tablets, capsules, and ophthalmic solutions. Its physicochemical properties, such as solubility, viscosity, and thermal gelation, can be tailored by modifying the degree of substitution and molecular weight, allowing for customization in drug formulation. The safety profile of HPMC is well-established, with minimal adverse effects reported, making it a preferred choice in pharmaceutical applications.

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[14] AFETY DATA SHEET Revision date: 18-Jul-2019 Revision Number 4

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United States Pharmacopeia and National Formulary (USP–NF) standards include guidelines on the proper storage and handling of pharmaceutical excipients like HPMC.
[34] ICH Guidelines (Q1A-Q1E)
The International Council for Harmonisation provides guidance on stability testing of new drug substances and products, which applies to excipients like HPMC under various environmental conditions.
[35] Google Patents (https://patents.google.com/): You can search for the patent numbers to view the full text and [technical details.
[36] WIPO PATENTSCOPE (https://patentscope.wipo.int/): A global database for patents from various countries.
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