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A REVIEW ON HPMC AS VERSATILE MATERIAL IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Nowadays HPMC (hydroxy propyl methyl cellulose) which is also known as Hypromellose most widely used polymer in various Pharmaceutical Dosage Forms. In different formulations due to its hydrophilic nature selected by the formulators. This review provides the idea not just about its hydrophilic matrix system rather more focus on advancements of recent formulations. This polymer provides maximum utilization of drug in a controlled manner and prolong the release rate of drug including therapeutic effects. HPMC have commercially different grades based on their different solid formulations, liquid formulations, gel preparations and bio-adhesive Preparations. This review also provides information about the HPMC as a Capsule shell material and with its dissolution studies maybe it can take place over hard gelatin capsules.

KEYWORDS: HPMC, Controlled release dosage forms, Hydrophilic, Pharmaceutical.

1. INTRODUCTION

HPMC is most popular matrix system because it is able to intended release for wide range of drugs. They are easily available, cost effective and easily accepted by formulators. The choice of polymer can affect the drug solubility, Chemistry and its viscosity as well. Suitable grades of HPMC will provide the broad range to formulators to design matrices. These formulations are generally considered as safe and it can be administered by the oral, buccal,

rectal including vaginal. This is stable Ph at the range of 3.0-11.0 and enzyme resistant as well. The history of HPMC is not clear however a US patent have been issued in 1960 to the Dow Chemical Company. HPMC swells and expand when it absorbs water. Its gelling point differs at the range of 50 °C to 90°C. Gelatin is commonly used to prepare capsules as a result of its solubility in biological fluid at body temperature and able to form homogenous film.[1] This review provides the problem and the solution of gelatin in case of capsule preparations. This review also serves as how can we enable the extremely short reaction in water.

2. Basic Properties of HPMC

- The empirical formula of HPMC is C8H15O8-(C10H18O6) n-C8H15O8.
- It is odourless and tasteless white fibrous powder.
- Stable in acidic and alkaline medium.
- It can be easily metabolised in the body and doesn't cause exothermic reaction.
- It is enzyme resistant and its viscosity depends on their different grades.

3. Thermal Properties[2]

Due to increase in temperature Hydration takes place. Decrease in relative viscosity as a result of hydration tends the polymer-polymer interactions of methoxy substituent. HPMC gets precipitate when increase in temperature. To identify this precipitation Light transmittance can be used which is up to 97.5%. When transmittance reaches 50% considered as the cloud point. It also depends on the HPMC concentration. At high concentration of HPMC gelling forms before turbidity but at low concentration turbidity observed first then gelation occurs. Electrolyte may decrease the thermal gelation and cloud point.

4. Mechanism of Action

Mainly diffusion and erosion are responsible for the drug release from matrices.[3]

- **Diffusion-** The movement of molecules under concentration gradient (high to low concentration) consider as diffusion.

- **Erosion-** The degradation of polymer in vitro due to change in polymer bond, pH and copolymer composition.

These two-mechanism based on the solubility of drugs if it is water soluble then drug released by diffusion and erosion of gel layer takes place but if its insoluble then erosion occurs.

5. Role of HPMC in Pharmaceutical Industry[4]

As a disintegrant

Generally, HPMC which have low viscosity grades used as a disintegrant and binder. For the granulation either dry or wet it requires the concentration between 2% and 5% W/W. Example: - E3-LV, K100-LV considered as low viscosity grades. K15 and K100 considered as high viscosity grades.

As film forming and Coating Material

To provide the better degree of hardness, friability, hygroscopicity, disintegration and for coating weight gain HPMC are generally used. It is also based on the viscosity. For aqueous film coating solutions low viscosity grades are used while organic solvents are used with high viscosity grades. 2-20%w/w HPMC concentrations are used to prepare coating solution for film coated tablets.

HPMC grade with Viscosity

Table: - 1 LV- Low Viscosity CR- Controlled Release.

USP Designation	HPMC Grade	Viscosity (cP)
2910	E3 Premium LV	3
2910	E5 Premium LV	5
2910	E6 Premium LV	6
2906	E4 M Premium	4000
2208	K3 Premium LV	3
2208	K4 M Premium	4000
2208	K4 M Premium CR	4000

As Bio-adhesive

Mainly the HPMC polymer materials Enhances the contact with mucus membrane through biological adhesion. It continues the slow release of drug for their specific treatment purpose. Through enhancement of penetration of intestinal epithelial cells, it changes the fluidity of gastrointestinal tract which consider as gastrointestinal biological adhesion technology and it also prolongs the retention time of pharmaceutical preparations in gastrointestinal tract.

As Topical material

In recent years gels are considered as safe, effective and low-cost preparation and easily compatible with various drugs. Percutaneous drug delivery system avoids the drug destroy in GIT suitable with Carbopol 980 and HPMC-K15m.

Now this review comes to its important part which provide the knowledge and information about actual versatility of Hydroxy Propyl Methyl Cellulose.

As Capsule shell material

Capsules are designed as oral administration of solid, semi-solid and liquid API (active pharmaceutical ingredient). They are enclosed with suitable excipients like Hard and soft gelatin and it provides the external protection like atmospheric oxygen, light, moisture and etc. Commonly gelatin is used as capsule shell material and they are suitable with biological fluid at body temperature and able to form strong homogenous shell.

6. Problems related with gelatin as capsule shell[5]

a) **Cross linking: -** Gelatin is a protein occurred naturally and it produces amino acid through hydrolysis. They are more reactive with aldehydes, metal ions, plasticizers and preservatives. Gelatin has amphoteric nature and it is incompatible with anionic and cationic polymeric excipients and surfactants and the excipient-excipient interaction cause the degradation with aldehydes. It can easily cross link with high temperature, high humidity and UV lights.

b) **Stability: -** Water acts as plasticizer in gelatin film and forms a flexible film. When relative humidity changes in the environment gelatin capsule shell gets soggy and this is major issue with gelatin shells in dry or humid climate.

c) **Temperature:** - When temperature falls down around 37°C solubility decreases and when it is down from 30°C shells are insoluble and gets distort. Therefore, every country has different limits in their pharmacopeia.

d) **Religious Perspective: -** In some of the area's animal source is a big concern for them such as vegans or vegetarians and those who are connected with some ethnic groups where forbid the animal products.

7. HPMC as an alternative[6]

As an alternative material some physicochemical and pharmaceutical property of HPMC.

a. It is derived from plant cellulose and semi-synthetic in nature.
b. To reduce the cross-linking problem with excipient, the polymer should free from amino acid.
c. When HPMC compares with gelatin as water intake it shows better stability at different temperature and moisture content.
d. HPMC capsules are easier to swallow than gelatin based.
e. According to 21 CFR 172.874 and regulation no1333/2008 permitted by USFDA as food additive for human consumption.
f. It is free from preservative, allergen, starch and gluten.
g. Some coloring agents can be used easily like iron pigments, titanium oxide, riboflavin and carmine etc.
h. The comparison of gelatin, HPMC have fast dissolution rate release of drug.

8. Manufacturing Process of HPMC empty capsule shells

Mainly capsules are formed by the mixing of Polymer with water and the specific colorants used then dip the mould pins in a right temperature of capsule shell material solution. After that drying, positioning and stripping are takes place, after the preparation of cap and body of the capsule they are ready to fill the drug and then after going to be polished and sealed.

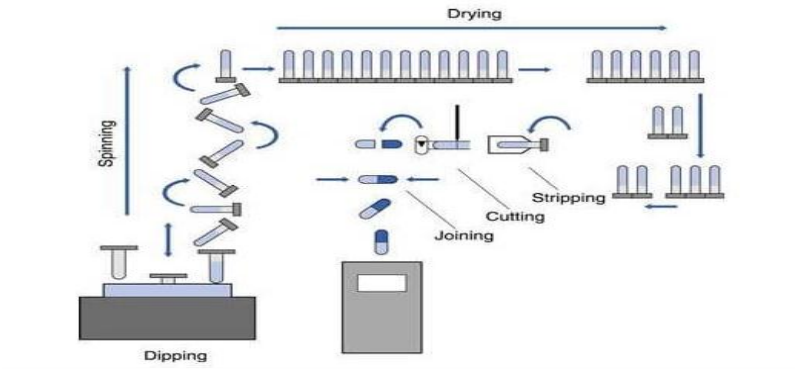

Fig: - 1 It is showing the capsule manufacturing process.

9. Factors affecting HPMC capsule shells[7]

Effect of temperature: - On the dissolution of HPMC and gelatin capsules it is observed that the temperature varies around 10-50°C but there was no effect on drug release even the pH was equal to 5.8. It shows the slower penetration of dissolution medium and gelatin capsules did not dissolve at 30°C.

Effect of size of capsule: - The major difference was found in dissolution of HPMC capsule size 0 and 3 but in another study no difference was found in HPMC capsules.

Bioavailability Studies: - In fasted and fed condition dogs plasma level observed that HPMC capsules have rapid T_{max} immediate release formulations, it indicates that for absorption the capsule shell was not rate limiting. On healthy human volunteers they found that T_{max} of about 1 hr at the disintegration of HPMC capsule at fasted condition.

Effect of Food interaction: - There are no specific indication of capsule shell interaction with food at addition of digestive enzymes either HPMC capsule or gelatin capsule but generally advised that HPMC capsule should administer to an empty stomach.

Sticking Tendency: - When it was tested on healthy male volunteers there was no sticking tendency observed either HPMC capsule shell or gelatin capsule shell but should be taken with upright body position with at least 50 ml water.

In vivo-in vitro correlation: - HPMC capsules may demonstrate low correlation between the in vitro dissolution/disintegration and the in vivo performance due to observed in vitro interaction between the medium and the HPMC capsule gelling systems, which is not seen in in vivo studies in animals or human volunteers.

To achieve better correlation, dissolution/disintegration testing specifications should be different from that of hard gelatin capsules. For hard gelatin capsules, 2-tier dissolution testing should be adopted and similar such modifications should also be employed during dissolution study from HPMC capsules.

Stability Studies: - In a study the HPMC capsule filled in a glass bottle and heated at various temperature for 24 hr and after that it kept at room temperature for 5 hr before the opening. The capsules were inspected visually and evaluated mechanical strength and disintegration dissolution profile but no visual observed in HPMC capsule.

How to enable HPMC reaction in short times?[8]

Mainly everybody always preferred water as a solvent which construct a strong chemical bond and it is easily available, nontoxic and environment compatible. Despite it is easily available and cheap it does not recommend as solvent because of its low solubility with organic materials. Mainly Micellar catalysis is followed to enable the chemistry in water.

HPMC has both hydrophilic and hydrophobic group. It enhances the viscosity in aqueous medium and mainly hydrophobic pockets could trigger this with nanoparticles via molecular shielding.

First the administered nanoparticle palladium HPMC pockets tested and then it is observed by high-resolution transmission electron microscopy, scanning transmission electron microscopy-based high-angle annular darkfield imaging and energy-dispersive X-ray spectroscopy mapping. Palladium observed ultrasmall and uniformly distributed and one molecule ligates with one palladium atom. To find out in situ cross linking formation of nanoparticles applied Buchwald-Hartwig reaction with aryls and bromide which is completed within 5 min and analyzed by gas chromatography mass spectroscopy and kept aside for 30 min and then 50 mol equivalent aryl and bromide suggests stable, active and fast reaction.

CONCLUSION

HPMC is most widely used due to its physical, chemical and biological properties. Despite of mostly used gelatin as capsule shell it has some demerits like storage condition and relative humidity but it can be overcome by HPMC. Many manufacturing companies found that HPMC capsules are suitable with all the excipients and drugs and stable at short term high temperature and flexibility even at low relative humidity. The catalytic reaction induces with the impact of two reaction methods like Buchwald Hartwig animations and peptide couplings. These two reactions shorten the reaction of HPMC in water. The HPMC has widely used by manufacturers but many researchers found dose dumping in tablets and as the research goes on HPMC on its properties and technology improvement new drug delivery system will discover but it requires more and more study based on its properties and stability.

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REFERENCES

1. Chinmaya Keshari Sahoo, HPMC a biomedical polymer in pharmaceutical dosage forms October-December, 2015; (875-880).

2. Callewaert, M., Millot, J., Lesage, J., Laurent-Maquin, D., and Edwards-Levy, F. “Serum Albumin-Alginate Coated Microspheres: Role of the Inner Gel in Binding and Release of the KRFK Peptide.” Intl. J. Pharm., 2009; 366 (1-2): 103-10.
3. Du Shouying et al J. Chem. Pharm. Res, The application of biomedical polymer material hydroxy propyl methyl cellulose (HPMC) in pharmaceutical preparations, 2014; 6(5): 155-160.
4. Sutapa Biswas Majee, Dhruti Avlani, Gopa Roy Biswas. HPMC as capsule shell material: physicochemical, pharmaceutical and biopharmaceutical properties. Int J Pharm Sci., 2017; 9(10): 1-6.
5. ACS Sustainable Chem. Eng., 2020; 8: 12612−12617.

   Website Fig 1- https://www.saintytec.com/hpmc-capsule/