WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 12, 2017-2024. **Research Article** ISSN 2277– 7105

EVALUATION OF HIGH VISCOSITY GRADES OF HYPROMELLOSE FOR THEIR POTENTIAL APPLICATION AS POLYMERS IN GASTRORETENTIVE DRUG DELIVERY SYSTEM

Dr. Rajashree Hirlekar*, Palak Phansalkar and Omkar Mainkar

Dept. of Pharmaceutics, Vivekanand Education Society's College of Pharmacy, Chembur, Mumbai – 400074, Maharashtra, India.

Article Received on
25 Oct 2015,

Revised on 15 Nov 2015,
Accepted on 05 Dec 2015

***Correspondence for Author**
Dr. Rajashree Hirlekar
Dept. of Pharmaceutics,
Vivekanand Education
Society's College of
Pharmacy, Chembur,
Mumbai – 400074,
Maharashtra, India.

ABSTRACT

Polymers are an important formulation consideration for Gastroretentive Drug Delivery System (GRDDS) as the polymers play an important role in allowing the dosage form to remain in gastrointestinal tract for a longer time thus enabling the required quantity of drug to be released and absorbed into the body. The objective of this study was to compare swelling, water uptake[1] and water holding capacity of commonly used grades of Hypromellose (Hydroxypropylmethyl cellulose) for their potential application as polymer for GRDDS. The study found that K100M grade of Hypromellose provided the best results which could facilitate its use as polymer in GRDDS.

KEYWORDS: Hypromellose, GRDDS, polymers.

INTRODUCTION

Drug candidates having absorption window in a particular region of GI tract are difficult to be designed as oral controlled release drug delivery systems. This is because only the drug released in the region preceding the window and vicinity of absorption window is available for absorption. The controlled release systems possessing the ability of being retained in the stomach are called gastroretentive drug delivery systems (GRDDS).[2] These systems help in optimizing the oral controlled release delivery of drugs having absorption window by continually releasing drug prior to absorption window, for prolonged period of time thus ensuring optimal bioavailability.

Excipients suitable for providing gastroretention

1. Biocompatible swelling agents[3]

Swelling refers to the uptake of water by a polymer system, with increase in volume. Swelling is often a prelude to polymer dissolution. However, swelling may occur without dissolution if water and the polymer are insufficiently compatible, if polymer chain length is sufficiently large, or if crosslinks are introduced to form a polymer network. The swelling process is analogous to osmosis, since water enters the polymer relatively rapidly, while dissolution of polymer into water, if it occurs, is comparatively slow because of the need for polymer chains to disentangle.

Depending on their structure, swelling agents can absorb aqueous or organic solutions. If the former is the case, a swelling agent is called a hydrogel. Since most swelling agents are hydrophilic in nature, they can absorb significant amounts of gaseous (moisture) or liquid water. The driving force for the absorption or swelling process is generally a balance of three forces of osmotic, electrostatic and entropy-favored dissolution of polymer in water. Three major elements control the swelling process of a hydrogel: the cross-link content, the ionic content and the hydrophilic content.

i. Cross-link content

Thermodynamically speaking, different states of matter may be assigned to the hydrogel molecules in water. For a non-cross-linked hydrogel, hydrogel molecules will eventually dissolve in water and occupy the whole volume, which is already occupied by water. In this way, non-cross-linked hydrogel chains behave like typical liquid molecules as they reach high entropy states by occupying the entire space. As the cross-link density increases, hydrogel molecules behave similar to semi-solid molecules with less entropy. At the extreme, when crosslink density is high, the hydrogel molecules behave like a solid with minimum entropy, which enables them to swell to minimum extent. Since entropy of the hydrogel molecules increases in water, the swelling of the hydrogel will be spontaneous if hydrogel molecules have sufficient mobility, which is dependent on the hydrogel cross-link density. Figure [1] depicts the entropy difference on hydration of non-cross-linked and cross-linked hydrogels.

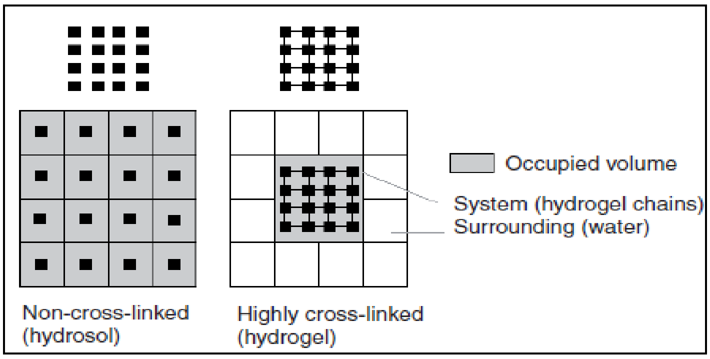

Figure [1]: Entropy Difference Between Non-Cross-Linked And Cross-Linked Hydrogels.

ii. Ionic content of the system and the surrounding

Structurally speaking, swellable hydrogels can be divided into two major groups: ionic and non-ionic. At a given amount of elastic forces, swelling of the ionic hydrogels will be a more entropy-favored process as opposed to their non-ionic counterparts. As the number of ions within the hydrogel structure increases, more and more osmotic and electrostatic forces will be created within the hydrogel structure. This forces a typical hydrogel to behave thermodynamically like a liquid as it occupies more space of the surroundings. On the other hand, changing the nature of the surroundings, which is water, can control the entropy-driven swelling process of the ionic hydrogel. Adding ions to the surroundings limits the swelling capacity of an ionic hydrogel and changes its state of matter. In other words, ionic hydrogel chains behave generally like solid and semi-solid molecules in the high and low ionic strength aqueous solutions, respectively.

iii. Hydrophilic content

The hydrophilic content of the hydrogel will affect the intermolecular forces responsible for diffusion and swelling. As hydrophilicity of the hydrogel increases, the interaction between water and hydrogel will increase too; this facilitates water diffusion and leads to greater swelling. Swellable systems are typically glassy polymers at room and body temperatures. Water uptake is initially resisted by the glass, but eventually it makes its way into the free volume at the surface. The glassy polymer at the surface relaxes to a configuration that is more compatible with water and swells. This permits water to intrude even further and a moving front is often observed separating a swollen outer layer from a dry inner core. Usually, swelling is accompanied by a glass-to-rubber transition.

Swelling dynamics are often complex and a variety of temporal release patterns are observed under swelling control. Under proper conditions, swelling, dissolution of polymer chains and drug release may occur simultaneously, further contributing to complexity.[4]

2. Superdisintegrants/Swelling Enhancers

Superdisintegrants are widely used in disintegrable dosage forms wherein they are physically dispersed within the matrix of the dosage form and expand when the dosage form is exposed to the wet environment. Swelling pressure and isotropic swelling of the particles create stress concentrated areas where a gradient of mechanical properties will exist. In fact, a mild explosion occurs at the stress-concentrated area by which the whole structure will break apart. The overall breakdown mechanism is shown in Figure [2].

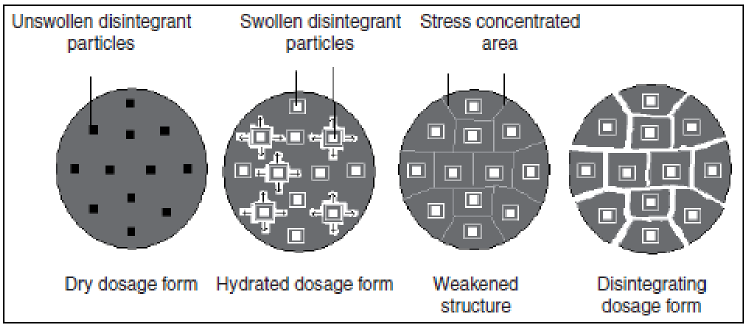

Figure [2]: Disintegration Mechanism of Superdisintegrant Materials.

MATERIALS AND METHODS

Materials

(A) Formulation.

i) Various grades of HPMC (Colorcon Ltd.) Table [1] lists the grades used in this study.

ii) Avicel PH102.

Table [1]: Materials, Chemistry and Molecular Weight.

Product	Chemistry	Molecular Weight
METHOCEL™		
K4M	HYPROMELLOSE 2208	4,000
K15M	HYPROMELLOSE 2208	15,000
K100M	HYPROMELLOSE 2208	100,000

(B) Reagents

i) 0.1 N HCl

ii) 0.01 N HCl

iii) 0.001 N HCl

Methods

25% w/w polymer compacts of Avicel PH 102 were made using Direct Compression process using Single punch tablet compression machine. The powders were added in order of increasing weight and the blending time was 10 minutes. A 12 mm circular flat punch used to make tablets.

a) Swelling study of polymer compacts

The swelling capacity of a polymer is related to its water uptake and water holding capacity and has an impact on its role in a swellable GR system. The swelling study here measures the increment in volume of the polymer at various time points due to swelling in presence of water. The volume of the tablets was measured using the formula

Volume = $3.14 \times R^2 \times H$, where R is the Radius of the tablet and H is the Height of the tablet measured using a Vernier Caliper.

Procedure

Compact tablets each of weight 500mg were made. These tablets contained 25% w/w polymer and Avicel PH 102 was used as an excipient. A tablet of each grade of polymer was placed in each of 100 mL solutions of 0.1N HCl, 0.01N HCl and 0.001N HCl at room temperature. The volume of the tablets was measured at 0, 15, 30, 60, 120, 180 and 240 minutes time points and percent increase in volume (Percent swelling) was calculated with respect to initial tablet volume.

Percent swelling = $(V_F - V_I) / V_I$

where V_F = Volume after 15, 30, 60, 120, 180, 240 minutes respectively.

where V_I = Volume after 0 minutes.

b) Water uptake and water holding capacity

The water uptake capacity is the ability of the material to draw water into its matrix while the water holding capacity is a measure of the ability of the material to immobilize water within its matrix.

Procedure

1. For determining water uptake capacity, tared centrifuge tubes with 0.5 g of material and 10 mL of distilled water were kept for 24 hours. The superficial water was decanted and

the tubes were reweighed. Water uptake capacity as g water/g material was calculated using the difference in the weights obtained.

Water Uptake Capacity = Weight of water (g)/Weight of material (g)

where Weight of water = Weight of tube after decantation – Weight of tube with sample.

2) The centrifugation and filtration method was used to compare the water holding capacity of the polymers. For the centrifugation method tared centrifuge tubes each containing the specified amounts (0.5g) of material soaked for 24 h in distilled water (10mL) were centrifuged at 4000 rpm for 20 min and the supernatant fraction was decanted. The fresh weight of material was determined and the water holding capacity was calculated as g water/g material.

Water Holding Capacity = Weight of water (g)/Weight of material (g)

where Weight of water = Weight of tube after centrifugation – Weight of tube with sample.

RESULTS AND DISCUSSION

Swelling and Erosion

Swelling in pure polymer compacts of HPMC occurs upon immediate hydration of the polymer. As the dry polymer becomes hydrated, the mobility of the polymer chains increase, thereby increasing the hydrodynamic volume of the polymer compact, which allows the compact to swell. As polymer chains become more hydrated and the gel becomes more dilute, the disentanglement concentration may be reached, i.e., the critical polymer concentration below which the polymer chains disentangle and detach from a gelled matrix. These events result in simultaneous swelling, dissolution and erosion.

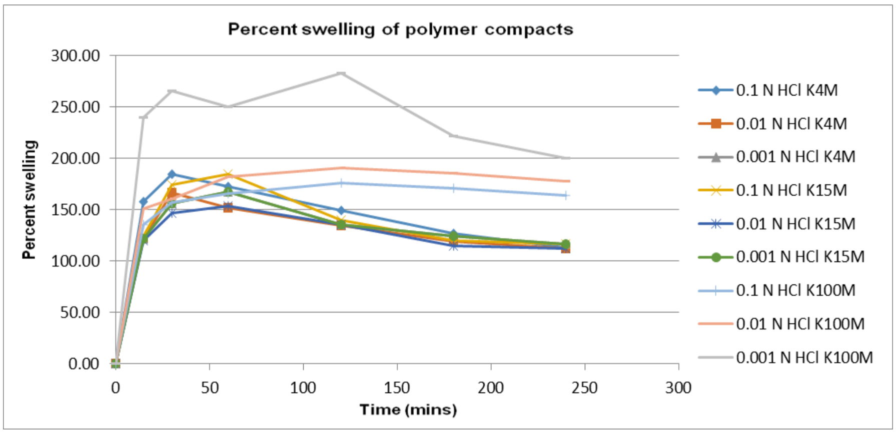

Figure 3: Comparison of Percent Swelling of Various Polymers.

High molecular weight polymers showed significantly greater swelling and less erosion than lower molecular weight polymers for HPMC. For K4M and K15M swelling was highest in high ionic strength solution (0.1N HCl) followed by 0.001N HCl and least in 0.01 N HCl. Thus swelling was found to increase with increase in ionic strength. The slightly higher swelling obtained in 0.001N HCl could possibly be due to decreased rate of erosion compared to 0.01N HCl. At time points 180 mins and later, the reduction in volume signaled the start of erosion.

For K100M swelling was highest in low ionic strength solution (0.001N HCl) followed by 0.01N HCl and least in 0.1 N HCl. Thus swelling was found to increase with decrease in ionic strength for K100M in contrast to K4M and K15M. The higher swelling obtained in 0.001N HCl could possibly be due to decreased rate of erosion compared to 0.01N HCl and 0.1N HCl. K100M showed a higher onset time to erosion which was only seen in 0.001N HCl.

Water uptake and Water holding capacity

Table 2 illustrates results of water uptake and holding capacity. It can be clearly seen that with increase in molecular weight, the water uptake and water holding capacity of polymer increases.

Table 2: Water Holding And Water Uptake Capacity Of Swelling Polymers.

Sr. No.	Polymer	Water uptake capacity	Water holding capacity
		(g water/g polymer)	
1.	K4M	7.54	6.81
2.	K15M	7.74	7.09
3.	K100M	8.22	7.34

CONCLUSION

The results obtained after evaluation of the polymers suggested that K100M polymer is best suited for GRDDS based on the floating principle. Thus, primary analysis of the polymer properties can be utilised for selecting the suitable candidate for GRDDS.

REFERENCES

1. Jain, N.K., Progress in Controlled and Novel Drug Delivery Systems, CBS Publishers and Distributors Pvt. Ltd., New Delhi. Pg. no.: 76-97.

2. Jain, N.K., Introduction to Novel Drug Delivery Systems, Vallabh Prakashan, New Delhi. Pg. no.: 35-39.
3. H. Omidian, K. Park. Swelling agents and devices in oral drug delivery J. DRUG DEL. SCI. TECH., 2008; 18(2): 83-93.
4. Ronald A. Siegel and Michael J. Rathbone, Chapter 2: Overview of Controlled Release Mechanisms, Fundamentals and Applications of Controlled Release Drug Delivery, Advances in Delivery Science and Technology, Controlled Release Society, 2012; 37.
5. Handbook of Pharmaceutical Excipients, 6th Edition, Pub- Pharmaceutical Press, London. Pg. no.: 326-329.