International Journal of Pharma and Bio Sciences V1(2)2010

THE EFFECT OF PLASTICIZER MOLECULAR WEIGHTS AND CONCENTRATIONS ON WATER VAPOR PERMEABILITY OF HYDROXY PROPYL METHYL CELLULOSE FILMS

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ABSTRACT

Plasticizers are added to improve the mechanical and conditional quality of film coating. However, other properties of coating solutions such as viscosity, droplet size and water vapor permeability (WVP) of free films be affected by incorporation of plasticizers. In this study, films of various viscosity grades of hydroxypropyl methylcellulose (HPMC) without and with different molecular weights (MWs) of polyethylene glycol (PEG) as plasticizer were prepared by a casting/solvent evaporation process and their water vapor permeability coefficient (R_{wvp}) were calculated. The results showed that, addition of 10% w/w PEG 200 caused a decrease in Rwvp of all grades of HPMC (E5, E15 and E50) free films and Rwvp increased by increasing the concentration of PEG 200 from 10% to 30% w/w. The R_{wvp} of HPMC E5 and E50 free films increased by increasing the PEG MW from 200 to 1500, but using higher MWs of PEG (4000 and 6000) caused to reduction of R_{wvp}. The conclusion could be drown that, as regards permeability, the addition of low MW of PEG as plasticizer at low concentration (10%) could be resulted to decrease of Rwvp of HPMC free films.

KEYWORDS

HPMC, plasticizer, aqueous film coating.

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INTRODUCTION

Polymers are used extensively in tablet coating formulations to mask bitter taste and protect ingredients from environmental extremes as well as aid in swallowing and enhancing appearance. Plasticizers are added to polymer film coating formulations to make the film more flexible and tougher. Plasticizers, which have molecular weights much smaller than the polymer's, enhance the mobility of the polymer molecules in the film. Therefore many of film mechanical and physical properties affect by adding the plasticizers e.g. glass transition temperature, viscoelastic behavior, elongation and permeability. The problems associated with organic solvent based film coating (cost, safety and environmental pollution) and the advantages of aqueous based systems have long been known. There is a tendency for industry to switch from organic coating to aqueous coating. HPMC, which is available in different degrees of substitution and viscosity designations, is one of most commonly used cellulose polymers in aqueous film coating. It is relatively easy to process due to its non-tacky nature. It is also cost effective and ideal to use as a polymer of low viscosity grade. Incorporation of polyethylene glycol, PEG, as a plasticizer into the film aqueous solution of HPMC resulted in increasing geometric mean diameter, which increased significantly with the inclusion of low MWs of PEGs[1]. Addition of PEG to HPMC films caused a decrease in both mechanical and thermomechanical properties, but lower grades were more effective than higher MWs[2]. It was shown that, using different plasticizers according to their plasticization efficiencies, could mainly affect the glass transition temperature values of HPMC[3]. As we have already reported, adding PEGs to HPMC solutions causes fundamental effects on viscoelastic behavior of coating solutions however the loss tangent of HPMC solution increase by increasing the MW of plasticizer[4]. PEG 400 was found to enhance WVP of HPMC free films[5]. WVP values of films were found to decrease with increasing MW of PEG up to 1000[6]. It was found that, the moisture permeation of HPMC films was slightly reduced by using S630 (a vinyl pyrolidon/vinyl acetate copolymer), but not to the same extent as polyetylen glycol[7]. It was shown that moisture permeability of HPMC films with and without plasticizer affected by adding the solid ingredients[8]. The effects of PEGs on WVP and mechanical properties of HPMC films prepared by using a pneumatic spraying technique were evaluated. The results showed that, the moisture permeability of films decreased slightly as compared to unplasticized control films with increasing MW of plasticizer[9]. The order of permeability decrease for plasticized cellulose acetate films PEG600>propylene glycol > dibutyle phetalate was reported in previous literature[10]. Studies on pharmaceutical film coatings have often examined the permeability to water vapor as well as the ability to provide mechanical protection for solid dosage forms. These properties are generally examined on free films prepared by casting or spraying techniques. Water vapor transmission properties of free films are evaluated by different methods. Permeability of low density polyethylene films were measured with a new method, based upon the measurement of the heat evaporation[11]. However often WVP through the free films are determined in a controlled environment by measuring the weight increase/decrease of desiccant/water, sealed in a glass vial with the tested film[12-14]. The present study was designed to investigate the effects of different MWs of PEGs (PEG 200, 400, 1500, 4000, 6000) on moisture permeability of various grades of HPMC (E5, 15, 50) films prepared from aqueous based solution.

EXPERIMENTAL

Materials

Methocel E5, E15, E50, hydroxypropyl methylcellulose (HPMC) were purchased from

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Colorcon, Ltd., UK. Polyethylene glycol (PEG) 300, 400, 1500, 4000, and 6000 were purchased from Merck & Co., Inc. and PEG 400 was also purchased from Sigma Chemical Co.

Methods

Preparation of HPMC solutions and films

The desired amount of HPMC, with and without various molecular weights of PEG, was weighted and mixed with approximately half of the desired hot distilled water. The remaining water was then added as cold water, mixed thoroughly, and the solutions left overnight. The concentration of PEG was kept constant at 10%, 20%, and 30% w/w of HPMC. The solutions were cast onto a clean glass plate by a thin layer chromatography applicator and left overnight to evaporate the solvent at room temperature. The film then peeled off and used for test.

Water vapor transmission (permeability)

A water vapor permeability cell was used to evaluate the permeability of the films. The method used was based on ASTM method E96-80-(1983). A diagrammatic representation of the Water – vapor permeability cell utilized is depicted in Fig. 1.

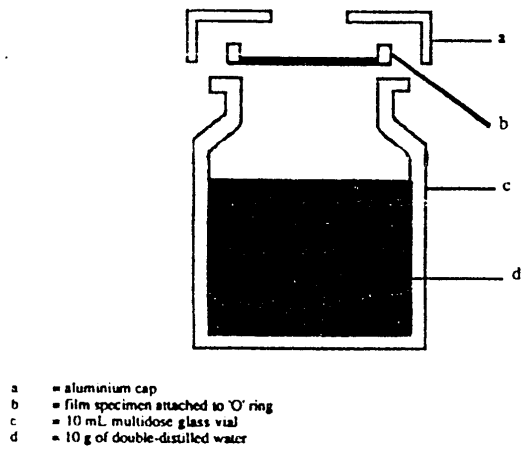

Fig. 1 ***Diagrammatic representation of the water-vapor permeability cell***

The rubber "O" rings with attached films were removed from the substrate surface and mounted directly on a 10ml multidose vial containing 10g of double–distilled water. The assembly was sealed by a standard aluminum cap. The water-vapor permeability cells were equilibrated for 12 hours at 20±0.5ºC within a dessicator containing silica gel. Once steady–state water vapor transfer had been achieved, the vials were removed and re-weighed at predetermined time intervals. The values of weight loss (kg), film thickness (m) and exposed surface area (m^2) were used to evaluate the water-vapor permeability coefficient of the films (see equation 1).

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$$R_{wvp} = \frac{W}{t} * \frac{1}{A} * T \qquad (1)$$

Where:

R_{wvp}=water-vapor permeability coefficient (kg/ms) and W/t=Slope of the weight loss verses time graph (kg/s)

Film thickness

Thickness of dried films was measured with a micrometer (No 2050-08 Mitutoyo Japan). Five measurements were taken on each specimen and their average was used in calculations.

Statistical analysis

Experimental results were expressed as mean ± SD. Student's t-test and one-way analysis of variance (ANOVA) were applied to check significant differences in R_{wvp}. Differences were considered to be statistically significant at $p < 0.05$.

RESULTS

After drying, HPMC films with more than 20% w/w of high MWs of plasticizers showed a non-homogeneous structure and incompatibility between HPMC and higher MWs of PEG. This incompatibility by incorporation of more than 20% w/w of high MWs of PEG1500, 4000 and 6000 exhibited by either opacity or spotting of films. Films which showed each of these interactions were omitted from the study. The graphs plotted for weight loss through the films versus time gave linear plots over the time course of the experiments indicating that a constant rate of water vapor transmission had been achieved (Fig. 2). R_{wvp} for each film was calculated by using slop of these linear plots and equation 1. Values of R_{wvp} with corresponding standard deviations are shown in Table 1a, b and c. each value shows the mean of at least 5 individual replicate determinations.

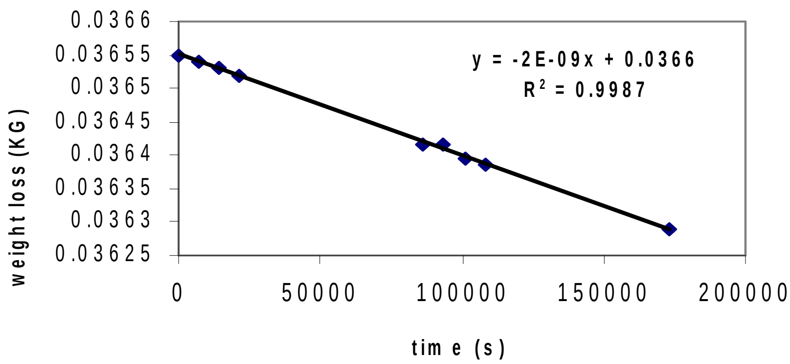

Fig. 2 ***Weight loss through the HPMC E15 film containing 20% PEG 400 versus time. R_{wvp} for each film was calculated by using slop of these linear plots and equation 1***

The moisture permeability of HPMC films was found to be dependent on both the amount and MW of added PEG. The results show that a significant decrease ($p < 0.05$) in R_{wvp} of HPMC E5 and E50 free films without plasticizer resulted when PEG 200 was added in 10% w/w on the other hand increasing the PEG 200

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concentration from 10% to 30% w/w resulted in Rwvp enhancement (Fig. 3). The results also show that, the R_{wvp} of HPMC E5 and E50 free films increased by increasing the PEG MW from 200 to 1500, but using higher MWs of PEG (4000 and 6000) caused to reduction of R_{wvp} (Fig. 4), but with HPMC E15 films, clear correlation was not observed between R_{wvp} and plasticizer concentration or MW.

Table 1.

The effect of PEG MWs on R_{wvp} of HPMC films: A- HPMC E5, B- HPMC E15 and C- HPMC E50.The R_{wvp} for these films without plasticizer is 2.98E-4, 2.81E^{-4} and 34E^{-4} for HPMC E5, E15 and E50, respectively

A:

P. concentration \ P. type	PEG 200	SD	PEG 400	SD	PEG 1500	SD	PEG 4000	SD	PEG 6000	SD
10%	8.54 E^{-5}	1.06 E^{-7}	1.74 E^{-4}	5.14 E^{-7}	1.86 E^{-4}	3.25 E^{-7}	9.3 E^{-5}	1.02 E^{-7}	8.54 E^{-5}	1.82 E^{-7}
20%	1.75 E^{-4}	2.12 E^{-7}	2.06 E^{-4}	5.36 E^{-7}	2.14 E^{-4}	4.92 E^{-7}	--------		-----------	
30%	2.85 E^{-4}	4.12 E^{-7}	2.91 E^{-4}	4.82 E^{-7}	2.96 E^{-4}	5.11 E^{-7}	---------		-----------	

B:

P. concentration \ P. type	PEG 200	SD	PEG 400	SD	PEG 1500	SD	PEG 4000	SD	PEG 6000	SD
10%	2.95 E^{-4}	6.26 E^{-7}	4.2 E^{-4}	3.65 E^{-7}	1.42 E^{-4}	2.26 E^{-7}	9.3 E^{-5}	1.11 E^{-7}	1.05 E^{-4}	1.08 E^{-7}
20%	2.73 E^{-4}	5.12 E^{-7}	3.67 E^{-4}	3.12 E^{-7}	3.47 E^{-4}	2.91 E^{-7}	---------		----------	
30%	3.10 E^{-4}	4.52 E^{-7}	2.61 E^{-4}	4.28 E^{-7}	---------		--------		---------	

C:

P. concentration \ P. type	PEG 200	SD	PEG 400	SD	PEG 1500	SD	PEG 4000	SD	PEG 6000	SD
10%	1.58 E^{-4}	4.81 E^{-7}	2.56 E^{-4}	4.12 E^{-7}	1.82 E^{-4}	5.19 E^{-7}	3.37 E^{-4}	3.46 E^{-7}	3.83 E^{-4}	4.22 E^{-7}
20%	2.86 E^{-4}	4.21 E^{-7}	3.25 E^{-4}	4.68 E^{-7}	1.46 E^{-4}	3.83 E^{-7}	----------		---------	
30%	4.12 E^{-4}	4.63 E^{-7}	4.02 E^{-4}	5.23 E^{-7}	---------		----------		----------	

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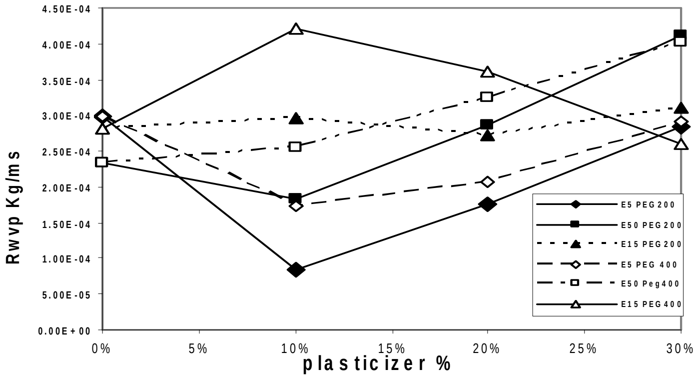

Fig. 3 *The effect of PEG low MWs concentration on R_{wvp} of HPMC E5, E15 and E50 free films*

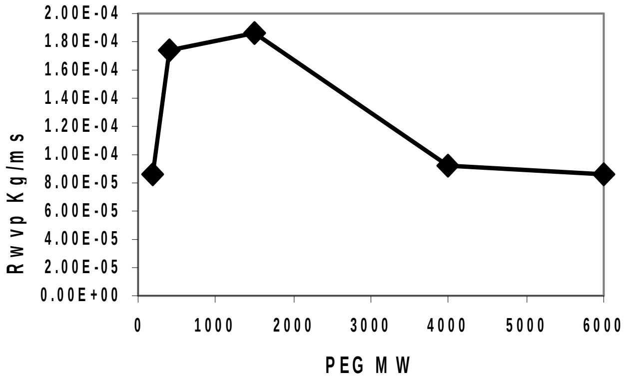

Fig. 4 *The effect of PEG MWs (10% w/w) on R_{wvp} of HPMC E5 free films*

DISCUSSION

The main factors which could affect the R_{wvp} of films are: The film and plasticizer hydrophilicity and compatibility between plasticizer and film former which could cause to produce more flexible film. According to the literature, a desirable pharmaceutical film coating is hard and tough without being brittle. The addition of plasticizer at lowest concentration of 10% resulted in strong film with a moderate elongation specially by using lower MWs of PEG [9]. The inclusion of low molecular weight of plasticizer resulted in the production of a smoother, more homogeneous film with less cracks. As the hydrophilicity of PEGs increase by decreasing MW, the higher MWs of PEG have more WVP resistance, thus substantially reducing the water barrier ability of films. On the other hands, although PEG with low MWs are more hydrophyl but using them in film formulation produced a film with less surface roughness and cracks causes to decrease of film WVP. These two different mechanisms could explain Figure 4 which indicates that, at first, from MW of 200 to 1500, the second mechanism mainly affects the WVP, but after 1500, the first mechanism could mainly affect the film WVP. The absence of correlation between Rwvp

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and plasticizer concentration/MW for HPMC E15, may be due to wider MW distribution of E15. As Rowe reported, polydispersity indices of 11.8, 71.5 and 18.1 were found for E5, E15 and E50 respectively [15]. Therefore, this polymer could show more self-plasticizing effect, and consequently more flexible film with less microscopic cracks, so in this case an increase in R_{wvp} occurred by inclusion of low MW of PEGs. This effect could be related to more hydrophilicity of film and then higher R_{wvp}.

CONCLUSIONS

This study has shown that incorporation of PEG as plasticizer into the HPMC E5 and E50 films made from aqueous solutions resulted in decreasing R_{wvp}. This effect related to either MW or concentration of plasticizers. These results could help us to choose the best plasticizer with suitable concentration in film coating process.

ACKNOWLEDGEMENTS

Financial support to this study was provided by Mazandaran University of Medical Sciences.

REFERENCES

1 Honary S, Orafai H and Shojaei A H, The influence of plasticizer molecular weight on spreading droplet size of HPMC aqueous solutions using an indirect method, Drug Develop Indus Pharm, 26: 1019-1024, (2000).
2 Honary S and Orafai H, The effect of different plasticizer molecular weights and concentrations on mechanical and thermomechanical properties of free films, Drug Develop Indus Pharm, 28: 711-715, (2002).
3 Hardy I J, Cook W G and Melia C D, Compression and compaction properties of plasticized high molecular weight hydroxypropyl methylcellulose (HPMC) as a hydrophilic matrix carrier. Inter J Pharm, 311 (1-2): 26-32, (2006).
4 Honary S and Gorkar M, Effect of polymer grade and plasticizer molecular weights on viscoelastic behavior of coating solutions, Iran J Pharm Res, 2: 125-127, (2003).
5 Johnson K, Hathaway R, Leung P and Franz R, Effect of triacetin and polyethylene glycol 400 on some physical properties of hydroxypropyl methylcellulose free films, Inter J Pharm, 7: 197-208, (1991).
6 Ayranci E, Buyuktas B S and Cetin E E, The effect of molecular weight of constituents on properties of cellulose-based edible films, Lebensmittel-wissenschaft und-technologie, 30: 101-104, (1997).
7 Kwok T S, Sunderland B V and Heng P W, An investigation on the influence of a vinyl pyrolidone/vinyl acetate copolymer on the moisture permeation, mechanical and adhesive properties of aqueous-based hydroxypropyl methylcellulose film coatings, Chem Pharm Bull , 52: 790-796, (2004).
8 Okhamafe A O and York P, Effect of solids-polymer interactions on the properties of some aqueous-based tablet film coating formulations. I. moisture permeability, Inter J Pharm 22: 265-272, (1984).
9 Heinamaki J T, Lehtola V M, Nikupaavo P and Yliruusi J K, The mechanical and moisture permeability properties of aqueous-based hydroxypropyl methylcellulose coating systems plasticized with polyethylene glycol, Inter J Pharm, 112: 191-196 (1994).
10 Rao P R and Diwan P V, Permeability studies of cellulose acetate free films for transdermal use: influence of plasticizers, Pharm acta helvetiae, 72: 47-51, (1997).
11 Hes L, Bernardo C A and Queiros M A, A new method for the determination of water-vapour permeability of polymer films based on the

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evaluation of the heat of evaporation, Polymer testing, 15: 189-201, (1996).

12 Tarvainen M, Sutinen R, Peltonen S, Tiihonen P and Paronen P, Starch acetate-a novel film-forming polymer for pharmaceutical coatings, J Pharm Sci, 91: 282-289 (2002).

13 Remunan-Lopez C and Bodmeier R, Mechanical and water vapor transmission properties of polysaccharide films, Drug Develop Indus Pharm, 22: 1201-1209 (1996).

14 Remunan-Lopez C and Bodmeier R, Mechanical, water uptake and permeability properties of crosslinked chitosan glutamate and alginate films, J Cont Release, 44: 215-225 (1997).

15 R C Rowe, The molecular weight and molecular weight distribution of hydroxypropyl methylcelluloseused in the film coating of tablets, J Pharm Pharm, 32: 116-119 (1980).