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COMMUNICATION

The Influence of Plasticizer Molecular Weight on Spreading Droplet Size of HPMC Aqueous Solutions Using an Indirect Method

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ABSTRACT

Film coating is a complex process that involves many factors. To ensure spreading and/or film capability, plasticizers are added. The role of different molecular weights of polyethylene glycol on the behavior of hydroxypropylmethylcellulose (HPMC) with different grades was determined and compared with values for the film without the plasticizer using a real method for spreading. The droplet size, distribution, and shape were analyzed as the criterion. The results show that the polymer grades and plasticizer types are important in droplet size formation.
Key Words: *Droplet size; Film coating; HPMC; Plasticizer.*

INTRODUCTION

Film coating is a process that needs comprehensive research and development. Studying the uniformity of atomized drops approaching the surface of the core is the critical and questioned state. Characterization of the uniformity and/or reproducibility of the process is crucial and is usually described as a degree of factors such as atomization, mean size, distribution, and spreading patterns. Definition of the extent and distribution of the atomized droplet on the surface is in turn complex. Several workers have carried out extensive experiments and methods to investigate factors affecting film coating. For example, Aulton and Twitchell (1), using a parallel laser

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beam of monochromatic light, discussed various aspects of atomization and solution properties in relation to film coating. They also found that the viscosity of the formulation and the momentum possessed by the droplet affect θc, the coating contact angles. The θc and droplet-spreading behavior in turn will influence the roughness and appearance of the coated product (2). In another work, Jusline et al. (3,4), using a pneumatic nozzle, showed the effect of three independent variables on droplet size distribution and spray angle. Their conclusion implied that high-pressure results in bimodal and narrow width distribution, and the amount of the binder, on the other hand, decreases the number of bimodal and increases the width of distribution. Their results also showed that the volume of small droplets is influenced more by applying a low concentration of polyvinylpyrrolidone (PVP) than a high concentration due to changes in viscosity. Comparing different techniques for droplet size measurement, Glover et al. and Musgrove and Beck (5,6) also determined advantages and disadvantages of different methods. Our study was designed to introduce a new and simple method to demonstrate the state of droplet distribution on the surface of a tablet bed. The results obtained from this method show a better match to the real condition in the film-coating process than the other methods.

EXPERIMENTAL

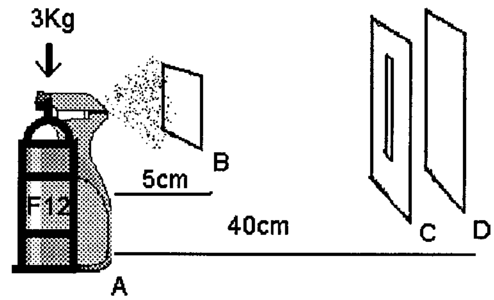
Materials

Methocel E5, E15, and E50 and HPMC were all purchased from Colorcon, Limited (London, UK). Polyethylene glycol (PEG) 300, 600, 1500, 4000, and 6000 were purchased from Merck and Company, Incorporated (Darmstadt, Germany). PEG400 was purchased from Sigma Chemical Company (St. Louis, MO).

Methods

Preparation of Hydroxypropylmethylcellulose Solutions

HPMC, with and without various molecular weights of PEG, was weighed and mixed with approximately half of the desired hot, colored distilled water. The remaining water was then added and mixed thoroughly, and the solutions were left overnight. HPMC solutions were transferred to the spray apparatus, which consisted of three parts (Picture1). The first was the spray gun containing F12, 100%, as a propellant. The spray rate constant was guaranteed by holding 3 kg weight on the top of the gun valve. The second part was the substrate sheet; a polyamide sheet was selected as a hydrophilic substrate and was held 40 cm from the gun perpendicular to the spray pattern beam and in a vertical position. A polyacetate transparent sheet with a 14 × 1 cm open slit was applied to allow a special region of the spraying pattern to reach the polyamide surface. The adhesion of the spread liquid on the sheet was achieved by reduction of the energy of the drop-substrate interface, which is in turn built up using a high-energy polymer such as polyamide. The third part was the beam barrier. An aluminum plate, 15 × 12 × 0.5 cm, was positioned between the gun and the sheet, 5 cm away from the gun. This barrier enabled the operator to allow a definite spray time.



Picture 1. A, Spray gun; B, beam barrier; C, polyacetate sheet with 14 × 1 cm slit; D, polyamide sheet.

Droplet Size Determination

Coating solutions were sprayed on the sheet at room temperature and placed in an oven at 40°C for 10 minutes. The sheet was then analyzed manually for droplet size using light microscopy.

Data Analysis

The overall diameters of at least 300 circular droplets and/or the mean of two Martin diameters of noncircular droplets were recorded in the vertical and horizontal directions. The most important statistical terms, geometric mean diameter, geometric standard deviation, and surface number mean, were recorded. The data were then analyzed and the relevant profiles were obtained.

RESULTS AND DISCUSSION

Method Evaluation

Reproducibility

Plotting droplet size frequency against droplet diameter for three identical experiments verified the accuracy

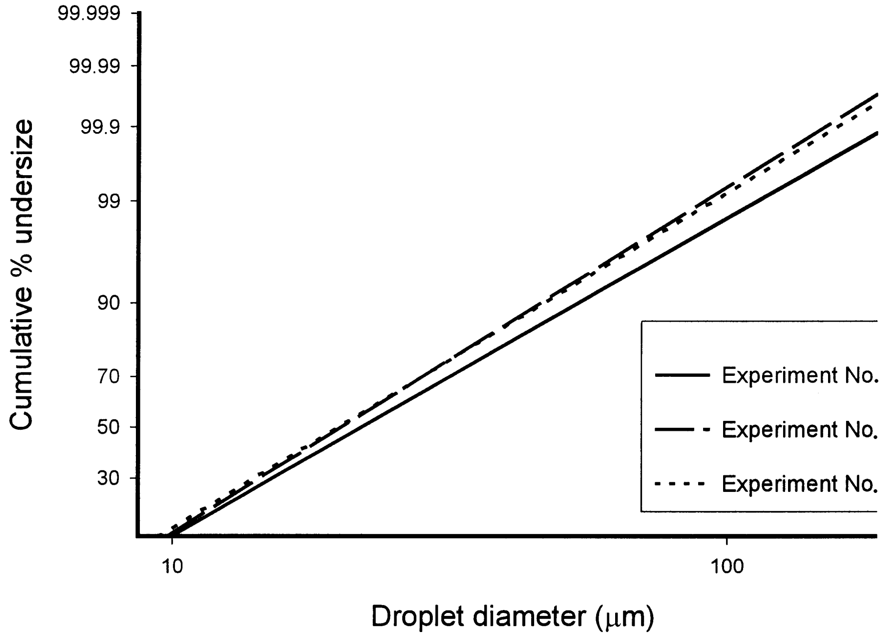


Figure 1. Three identical experiments for HPMC E5, 2% (w/v).

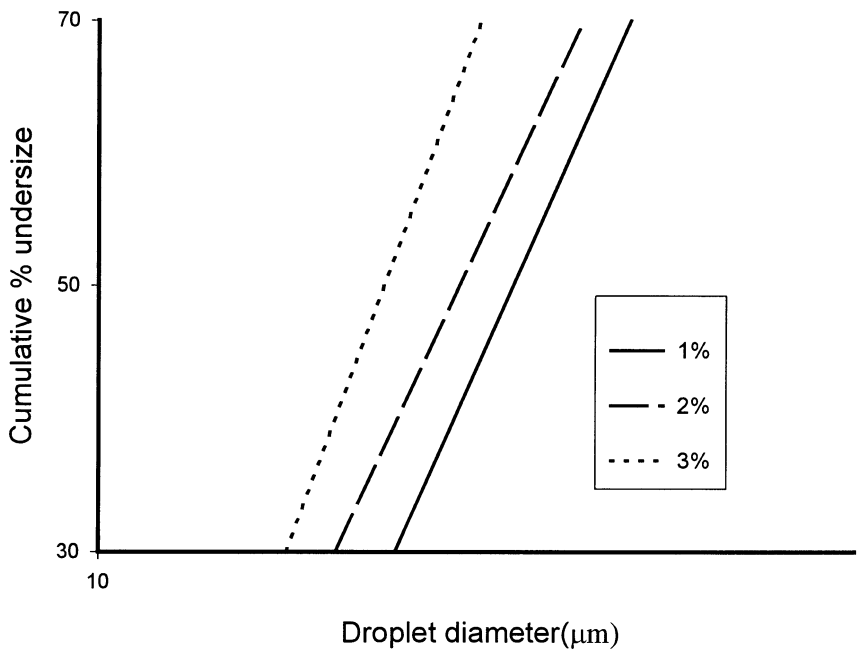


Figure 2. The effect of HPMC E15 solution concentration on the droplet size.

Table 1

Geometric Mean Diameter and Geometric Standard Deviation of Different Solution Concentrations of the Same Polymer

HPMC 15% (w/v)	Dg μm	σg *10
1	35	1.94
2	29.5	2.03
3	22.5	1.67

of the method. One-way analysis of variance (ANOVA) indicated no significant difference ($p > .05$) in size distribution of droplets produced under the same conditions. The results for two different sets of these experiments are shown in Fig. 1. Analyses of the obtained data using different concentrations of same viscosity grade of polymer (Fig. 2) showed a significant difference ($p < .05$) in diameter of droplet produced (Table 1).

A number of other methods, such as laser diffractometry, have already been used to study droplet size directly (7). It was shown in those studies that droplet size would increase as the viscosity of the solution was enhanced. However, measurement of droplet size on a more appropriate surface seems to be a better approach since the spreading properties of the film-coating solution are also determined. As a result, this approach is closer to the real condition in film-coating processes.

Region of Droplet Size Measurement

The results of all recorded horizontal and vertical direction values were plotted as shown in Fig. 3, indicating the uniformity of the distribution, at least in the two investigated directions. The correlation showed good reproducibility of the process parameters used in the method.

These results showed a significant difference between recorded peaks on the vertical and horizontal scales ($p < .05$) Horizontal records were more similar and had a narrower distribution than the verticals. The reason is that the spray pattern distributes along the vertical position in the direction of gravity; the upper droplets are lighter, while the lower are heavier and bigger. Therefore, the horizontal raw data are more similar and have less standard deviation than the vertical data.

Effect of Viscosity Grade of Polymer on Droplet Size

Plotting the cumulative percentage undersize against droplet diameter for the same concentration (1%) of three

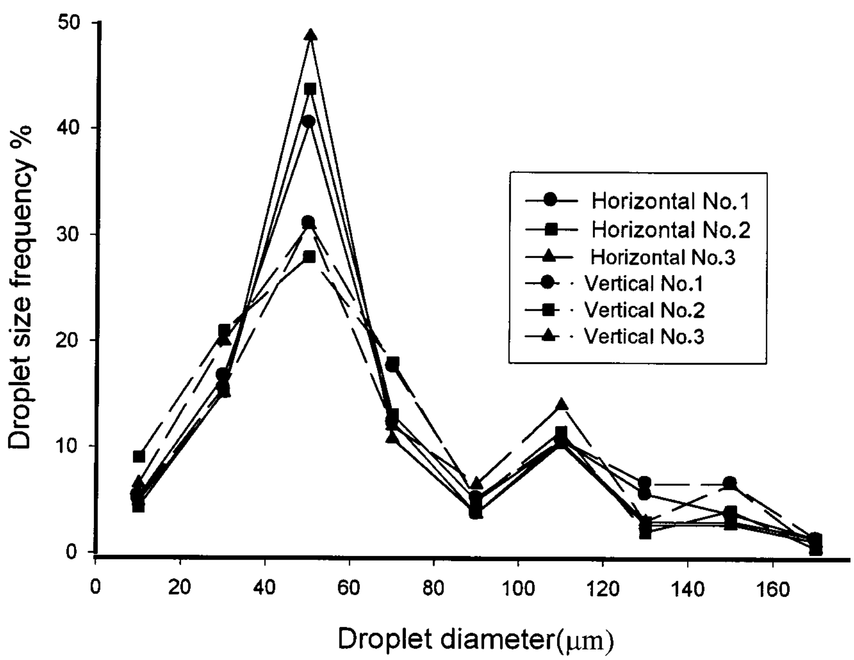


Figure 3. Vertical and horizontal record of three identical experiments for HPMC E50 1% (w/v).

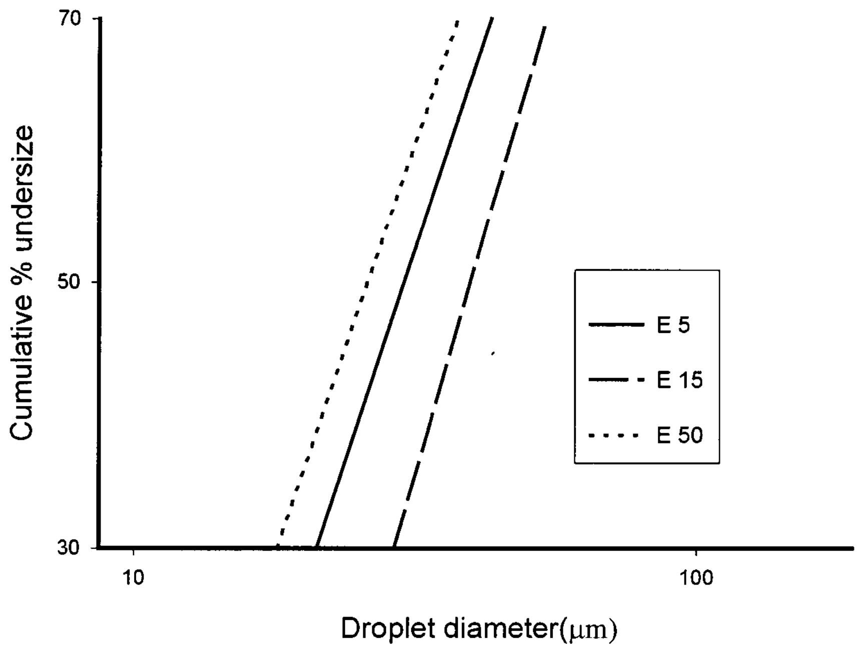


Figure 4. The effect of 1% w/v solution of three different viscosity grades of HPMC.

different viscosity grades of HPMC (E5, E15, E50) showed a significant difference ($p < .05$) in droplet diameter produced (Fig. 4). The data obtained also illustrate that the geometric mean diameter of droplets produced from E15 solution is higher than for the other viscosity grades of HPMC (E5 and E50) (Table 2).

There are two main factors that influence the size of droplets in the method used in our study: formation and spreading of droplets. As Fig. 5 shows, increasing the viscosity grade of polymer in the case of E5 and E50 resulted in a decreased geometric mean diameter of droplets. The high viscosity of E50 solution will cause less spreading of droplets on the substrate surface. This could also be related to less molecular freedom and less self-plasticizing properties of E50 in comparison to E5. On the other hand, the same data show an increase of geometric mean diameter of droplets using E15 rather than E5 and E50. As Rowe reported (7), E15 has a wider molecular weight distribution. Polydispersity indices of 11.8, 71.5, and 18.1 were found for E5, E15, and E50, respectively. Therefore, this polymer could show more self-plasticizing effect, and consequently more spreading effects, than E5 and E50. Also, it can form bigger droplets than E5 as a result of high viscosity.

Table 2

Geometric Mean Diameters and Geometric Standard Deviation of Three Different Viscosity Grade Solutions 1% (w/v)

HPMC Grades	Dg μm	σg *10
E5	29.9	1.99
E15	38.5	1.75
E50	25.2	2.01

Effect of Plasticizer on Droplet Size

Incorporation of PEG as a plasticizer into the aqueous solutions of HPMC resulted in increasing geometric mean diameter. Comparing different molecular weights of PEG, the geometric mean diameter increased more significantly ($p < .05$) with the inclusion of low molecular weights (300,400) than with high molecular weights of PEGs. Higher molecular weight species of PEG do not show as much increase in geometric mean diameter as lower molecular weight PEGs (Fig. 5) due to reduction in the mole fraction of plasticizer to the polymer; as a consequence, fewer plasticizer molecules are available to facilitate movement and spreading of HPMC (Table 3).

Our results show that the addition of plasticizer would increase the geometric mean diameter, which could be

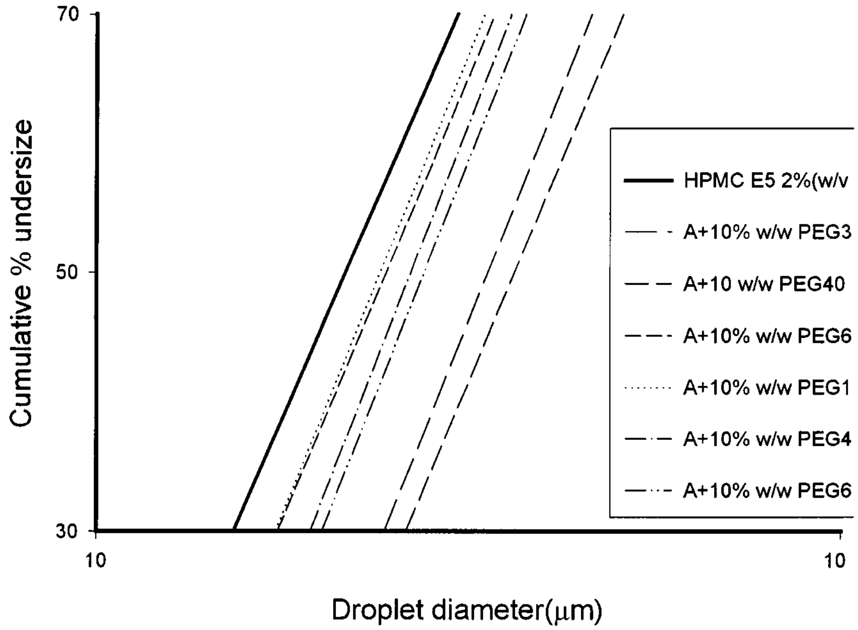


Figure 5. The effect of plasticizer type on the droplet size.

Table 3

Geometric Mean Diameter and Geometric Standard Deviation of HPMC E5 With and Without Different Platicizers

Samples	Dg μm	σg *10
HPMC E5 2% (w/v)-A	21.5	1.87
A + 10% w/w PEG 300	32	1.78
A + 10% w/w PEG 400	37	1.95
A + 10% w/w PEG 600	24	1.85
A + 10% w/w PEG1500	23	1.77
A + 10% w/w PEG4000	26	1.76
A + 10% w/w PEG6000	27	1.78

attributed to the increase in mobility and spreading properties of droplets on the substrate surface.

CONCLUSION

Our results show that the method used has good reproducibility and validity and is more compatible with the real condition. Polymer grade and plasticizer types have an important role in droplet formation and spreading, which in turn influences the appearance of the coated product in terms of film coating.

ACKNOWLEDGMENT

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