



# Multi-Layer Films Prepared by Spray Coating for Effervescent Floating Tablets

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## ABSTRACT

This study proposed the preparation process for multi-layer films by spraying technique. The films were evaluated for mechanical properties, water contact angle and water vapor permeability for the development of effervescent floating tablets. The films consisted of 2 layers: a gas-forming layer and a gas-entrapped layer.  $\text{NaHCO}_3$ : HPMC (8:2) mixture was used as a gas-forming layer. Eudragit® RL 30D plasticized with diethyl phthalate was used as the gas-entrapped layer. Multi-layer films were successfully prepared by spraying technique on Teflon cubes from 2 to 10 layers. The coating weight gain was 12% w/w for the gas-forming layer and 10% w,w for the gas-entrapped layer. Increasing the number of layers enhanced puncture strength and elongation in the dry and wet states. However, the film's flexibility was decreased at 10 layers due to the thickness of each layer. The increasing number of layers led to decreasing water contact angle and enhancing water vapor permeability coefficient suggesting the improvement of solvent penetration through the film.

**Keywords:** Multi-layer film; Puncture test; Spray coating; Water contact angle; Water vapor permeability

## 1. Introduction

The multi-layer coating technique has been developed and applied in drug delivery systems [1]. This technique provides many benefits, such as the ability to control drug release at a constant rate and improvement of the desirable properties of the drug delivery systems [2-4]. Sungthongjeen et al. previously developed floating multi-layer coated tablets using a

multi-layer coating technique [5]. The tablet was coated by 2 coating layers: a gas-forming layer and a gas-entrapped layer. The gas-entrapped layer should have a high-water permeability for a shorter time to float. To avoid the film rupturing from the inner air pressure, good flexibility of the film was required. The film properties played a crucial role in the floating properties.

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Free films are commonly used to evaluate the properties of coating films. Film preparation method is the main factor that affects the films' properties [6]. Casting and spraying methods are the general techniques for film preparation. However, the casting method was not suitable for the preparation of multi-layer films because the coating solution of the second layer might dissolve or interact with the first layer [7]. To overcome this obstacle, the film needs to be prepared by the spraying method. This technique can make a uniform and reproducible film [7, 8].

This study aimed to propose a preparation process for multi-layer films by spraying technique and to evaluate mechanical properties, water contact angle and water vapor permeability of the films for the development of effervescent floating tablets.

## 2. Materials and Methods

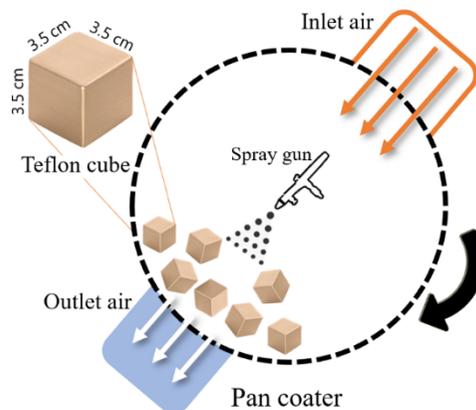
### 2.1 Materials

Eudragit® RL 30D (Evonik Industries AG, Essen, Germany) was used as a gas-entrapped layer. Diethyl phthalate was purchased from Sigma-Aldrich Chemie GmbH, Germany. Sodium bicarbonate (Fisher Scientific UK Limited, Leicestershire, UK) and hydroxypropyl methylcellulose, HPMC (Anycoat AN15, Samsung Fine Chemical Co. Ltd., Ulsan, Korea) were used as a gas-forming layer. Polyethylene glycol 6000 was supplied by Fluka Chemical Corp., Buchs, Switzerland. All other chemicals were analytical grade.

### 2.2 Preparation of multi-layer films

The multi-layer film was prepared by spraying technique (Fig. 1). The film designed for the effervescent floating tablet contained 2 types of coating layers. For the gas-forming layer, sodium bicarbonate was incorporated into HPMC solution with the ratio 8:2. The mixture was plasticized with PEG 6000 (10% w/w based on the solid content). Eudragit® RL 30D plasticized with 20% w/w DEP was a gas-entrapped layer. The 2 types of coating layers were

subsequently sprayed onto the Teflon cube using perforated pan coater (NR-COTA18, N.R. Industries Co., Ltd., Bangkok, Thailand). The layer-by-layer technique was used for the film spraying.



**Fig. 1.** Scheme of multi-layer film preparation using a spraying technique.

The coating levels of gas-forming layers and gas-entrapped layers are presented in Table 1. The conditions for film spraying were as follows: inlet temperature, 48 - 50 °C; outlet temperature, 38-40 °C; atomizing air pressure, 1 bar; spray rate, 5-10 mL/min. Once the desired coating level was achieved, the films were dried in the coating chamber for 30 min at 48-50 °C prior to spraying the next layer.

**Table 1.** Coating levels of gas-forming layers and gas-entrapped layers in the multi-layer film preparation.

Coating layer	Multi-layer film (%w/w)				
	F1	F2	F3	F4	F5
1. Gas-forming layer	10.0	5.0	3.3	2.5	2.0
2. Gas-entrapped layer	12.0	6.0	4.0	3.0	2.4
3. Gas-forming layer	-	5.0	3.3	2.5	2.0
4. Gas-entrapped layer	-	6.0	4.0	3.0	2.4
5. Gas-forming layer	-	-	3.3	2.5	2.0
6. Gas-entrapped layer	-	-	4.0	3.0	2.4
7. Gas-forming layer	-	-	-	2.5	2.0
8. Gas-entrapped layer	-	-	-	3.0	2.4
9. Gas-forming layer	-	-	-	-	2.0
10. Gas-entrapped layer	-	-	-	-	2.4

After spraying the final layer and drying, the films were removed from the cubes. The thickness of films was determined in five positions with a thickness gauge

(Mini-test 600B, Erichsen, Hemer, Germany). The multi-layer films were kept in an airtight container in a desiccator over silica gel until they were required for further study.

## 2.3 Evaluation of multi-layer films

### 2.3.1 Scanning electron microscope

Scanning electron microscope (SEM) (LEO 1455 VP, Zeiss, Jena, Germany) was used to characterize the morphology and cross-section of films. The samples were coated with gold and mounted in a sample holder. The photomicrographs of the samples were taken at an acceleration voltage of 15 kV at 100x to 200x magnifications.

### 2.3.2 Mechanical properties

The mechanical properties of the films were measured by a puncture test using a texture analyzer (TA.XT.plus, Texture Analyzer, Stable Micro Systems, UK). A stainless-steel puncturing probe with a spherical end (diameter 5 mm) was driven through the film with a speed of 0.1 mm/s. Force–displacement curves were recorded. The dry and wet films were investigated. To simulate the condition in the stomach, the film in the wet state was immersed in the 0.1 N HCl for 5 min prior to the test. The force at break and the maximum displacement of the films were measured and converted to puncture strength and elongation at puncture [9].

$$\text{Puncture strength} = \frac{F}{A_{cs}}, \quad (2.1)$$

where  $F$  is the load required for puncture,  $A_{cs}$  is cross-sectional area of the edge of the dry film located in the path of cylindrical opening of the film holder ( $A_{cs} = 2rd$ , where  $r$  is the radius of the hole,  $d$  is the thickness of the film).

$$\text{Elongation} = \frac{\sqrt{r^2 + D^2} - r}{r} \times 100, \quad (2.2)$$

where  $r$  is the radius of the film exposed in the cylindrical hole of the film holder and  $D$

is the displacement of the probe from point of contact to the point of film puncture.

### 2.3.3 Water contact angle

The contact angle goniometer (OCA20, Dataphysics, Regensburg, Germany) was used to measure water contact angle of the film. The 5.0  $\mu\text{L}$  of purified water was gently dropped on the outer layer of the films (gas-entrapped layer) using a microsyringe. The angle between the tangent line and the film surface was recorded at 0, 10, 30, 60, 90 and 120 s.

### 2.3.4 Water vapor permeability (WVP)

The film was placed on an open 4-mL glass vial containing 4 g of granular calcium chloride, and was then covered with an aluminum cap with an opened circular hole diameter of 1.3 cm (test area, 1.33  $\text{cm}^2$ ). The vials were conditioned in a desiccator containing silica gel for 24 h. The vials were weighed and placed in a desiccator containing a saturated aqueous NaCl solution (75% RH, 27 $\pm$ 2 $^\circ\text{C}$ ). Then, reweighing of the vials was done at designated intervals (24, 48, 72, 96 and 120 h). The WVP coefficient was calculated using Eq. 2.3.

$$\text{WVP} = \frac{W \times T}{A \times \Delta P}, \quad (2.3)$$

where  $W$  is the amount of water permeated through the film in mg/h,  $t$  is the thickness of film (mm),  $A$  is test area ( $\text{mm}^2$ ), and  $\Delta P$  is the vapor pressure difference (mmHg).

## 2.4 Data analysis

The difference in average of data was compared by analysis of variance (one-way ANOVA). The significance of the difference was determined at 95% confident limit ( $\alpha = 0.05$ ).

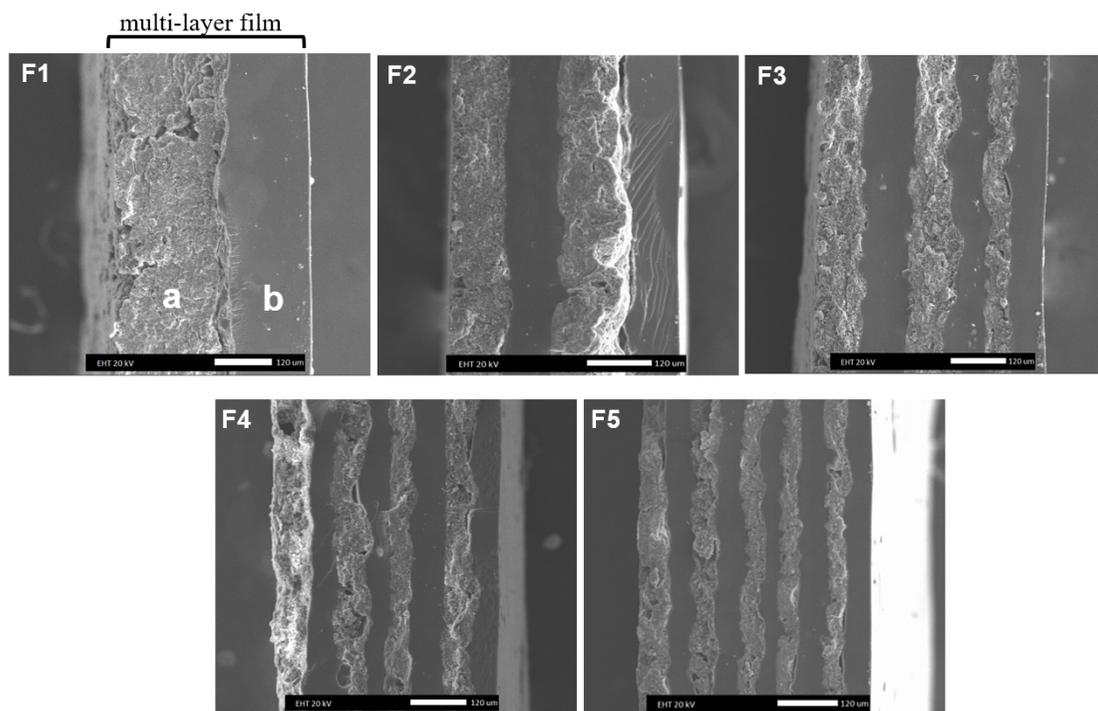
## 3. Results and Discussion

### 3.1 Multi-layer film

The multi-layer film was successfully prepared on the Teflon cubes by spraying

method using a perforated pan coater. The film's surface was smooth. The thicknesses of the multi-layer films were in the range of 0.49-0.52 mm. The weights were 57.24-59.21 mg/cm<sup>2</sup>. Fig. 2 exhibits a cross-sectional morphology of multi-layer films. The gas-forming layer (a) is the light gray which showed the rough texture due to

sodium bicarbonate in HPMC. The homogenous dark gray layer (b) is the gas-entrapped layer prepared by the Eudragit<sup>®</sup> RL 30D. Each layer of the film was distinctly separated, which indicated that the coating solution of each layer could be dried, and the films were completely formed.



**Fig. 2.** The cross-sectional morphology of the multi-layer films: (a) gas-forming layer and (b) gas-entrapped layer.

### 3.2 Mechanical properties of the multi-layer films

The gas-entrapped layer for an effervescent floating system should be flexible to withstand air pressure in the system and prevent early rupture of the layer [5]. Puncture strength and elongation are the parameters that indicate the film properties. There are two conditions for the puncture test: dry and wet states. Film in the dry state could be measured to predict the performance of the final coated tableted from under applied stress (e.g., compression, shipment) [10]. In the wet state, the condition

was simulated gastric fluid in the stomach. Puncture strength of the films indicates a toughness of films. Elongation of the films indicates a flexibility of films. A high puncture strength and elongation are good mechanical properties for the gas-entrapped layer of the effervescent floating system.

The effect of increasing the number of film layers on the mechanical properties of multi-layer films is illustrated in Fig. 3. Increasing the number of layers did not change puncture strength of the films (Fig. 3a). The film elongation tended to increase, indicating an increase in the flexibility and

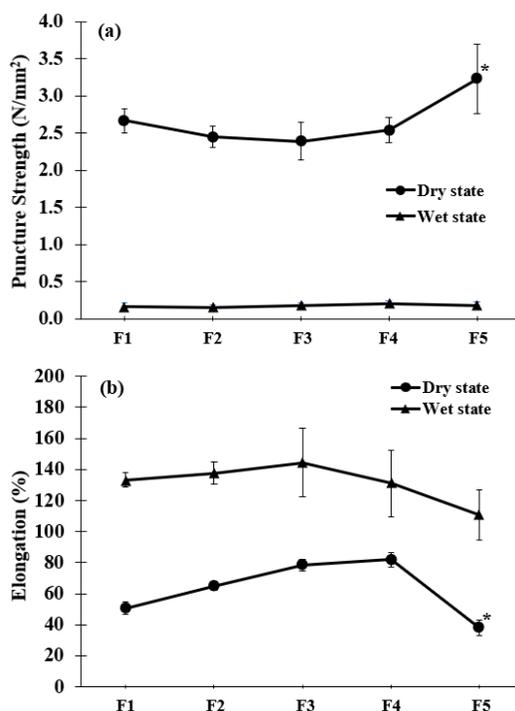
stretchability of films (Fig. 3b). However, the 10-layer film (F5) exhibited more brittle properties, which had significantly higher puncture strength and lower elongation ( $p < 0.05$ ).

In the wet state, film elongation tended to decline slightly by increasing the number of layers. This behavior might be explained by the thickness of the coating layers. The multilayer structure led to low thickness in each layer (Fig. 2). In a thinner layer, the polymer matrix is loose and low in inter and intramolecular interactions and, consequently, less resistant to rupture [11].

Films in the wet state clearly exhibited a decrease in puncture strength (Fig. 3 a). This is due to the erosion of the gas-forming layer when the film was contacted with 0.1 N HCl. The elongation of films highly increased when compared to the dry state. This phenomenon is explained by the plasticizer effect of water molecules. When the films were hydrated, there was the interference of water with the interchain hydrogen bonding leading to a decrease in puncture strength and increase in flexibility [12].

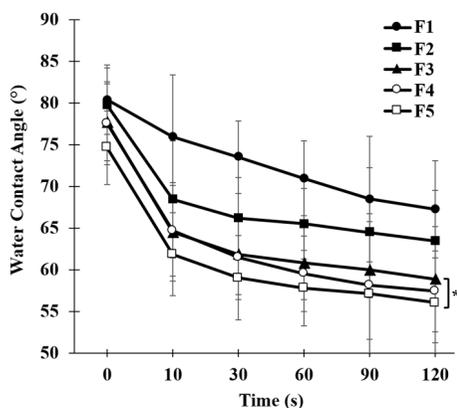
### 3.3 Water contact angle

The water contact angle is the parameter that reflects the degree of hydrophobicity and hydrophilicity of surface [12]. The films for effervescent floating systems must be wettable enough to permit water penetration into the floating tablet.



**Fig. 3.** Puncture strength (a) and elongation (b) of multi-layer films in dry state and wet state ( $n=6$ ).

The water contact angles on the multi-layer films at 0, 10, 30, 60, 90 and 120 s are presented in Fig. 4. The water contact angles of multi-layer films at 0 s were less than  $90^\circ$ , suggesting that the films had a hydrophilic nature surface or good wettability [13]. Interestingly, the water contact angle was decreased as the number of layers increased. Additionally, increasing the number of layers (F3-F5) showed less water contact angle as a function of time than F1 and F2.

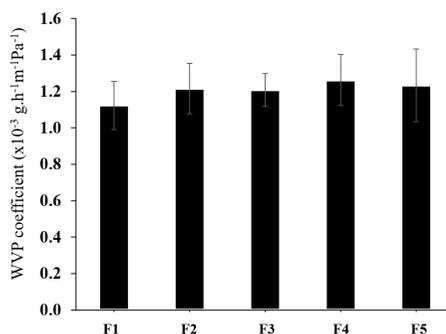


**Fig. 4.** Water contact angles of the multi-layer films at 0, 10, 30, 60, 90 and 120 s ( $n = 9$ ).

The reduction in water contact angle as a function of time indicated the water penetration through surface of the polymer [13]. Increasing the number of layers significantly decreased water contact angle over time ( $p < 0.05$ ). This result shows that increasing the number of layers tended to increase solvent penetration through the film due to the reduction of thickness of the outermost layer [14].

### 3.4 Water vapor permeability

WVP coefficient is a parameter that can predict water permeation through the films. Fig.5 shows that increasing the number of layers slightly tended to increase the WVP coefficient suggesting an increase in the hydrophilicity of the film. This might be because the multilayer structure led to less dense film structures [15].



**Fig. 5.** Water vapor permeability coefficient of the multi-layer films ( $n = 6$ ).

This result was consistent with the enhanced wettability and hydrophilicity of the films as reported by the water contact angle. Zheng et al. [16] reported that the WVP of Eudragit RS 30 D film could be enhanced by adding hydroxyethyl cellulose. This improved the hydrophilicity of the films.

## 4. Conclusion

The preparation of multi-layer film by spraying method in a perforated pan coater exhibited complete film formation. An increasing number of gas-forming and gas-entrapped layers demonstrated higher mechanical properties. The water contact angle was decreased by increasing the number of layers. Increasing the number of layers also improved the water vapor permeability coefficient. Therefore, the multi-layer films allowed solvent to penetrate through the film faster. Finally, these findings are useful for multi-layer films preparation and multi-layer effervescent floating tablets studies.

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## References

- [1] Dekyndt B, Verin J, Neut C, Siepmann F, Siepmann J. How to easily provide zero order release of freely soluble drugs from coated pellets. *Int J Pharm* 2015;478(1):31-8.
- [2] Yadav G, Bansal M, Thakur N, Khare S, Khare P. Multilayer tablets and their drug release kinetic models for oral controlled drug delivery system. *ME J Sci Res* 2013;16:782-95.

- [3] Dekyndt B, Verin J, Neut C, Siepmann F, Siepmann J. How to easily provide zero order release of freely soluble drugs from coated pellets. *Int J Pharm* 2015;478(1):31-8.
- [4] Weiss M, Kriangkrai W, Sungthongjeen S. An empirical model for dissolution profile and its application to floating dosage forms. *Eur J Pharm Sci* 2014;56(1):87-91.
- [5] Sungthongjeen S, Sriamornsak P, Puttipipatkachorn S. Design and evaluation of floating multi-layer coated tablets based on gas formation. *Eur J Pharm Biopharm* 2008;69(1):255-63.
- [6] Yaseen M, Ashton HE. Effect of method of free film preparation on physical properties of organic coatings. *National Research Council Canada*; 1976.
- [7] Mendoza-Romero L, Piñón-Segundo E, Nava-Arzaluz MG, Ganem-Quintanar A, Cordero-Sánchez S, Quintanar-Guerrero D. Comparison of pharmaceutical films prepared from aqueous polymeric dispersions using the cast method and the spraying technique. *Colloids Surf A Physicochem Eng Asp* 2009;337(1-3):109-16.
- [8] Obara S, McGinity JW. Influence of processing variables on the properties of free films prepared from aqueous polymeric dispersions by a spray technique. *Int J Pharm* 1995;126(1-2):1-10.
- [9] Kriangkrai W, Puttipipatkachorn S, Sriamornsak P, Pongjanyakul T, Sungthongjeen S. Impact of anti-tacking agents on properties of gas-entrapped membrane and effervescent floating tablets. *AAPS PharmSciTech* 2014;15(6):1357-69.
- [10] Bodmeier R, Paeratakul O. Mechanical properties of dry and wet cellulosic and acrylic films prepared from aqueous colloidal polymer dispersions used in the coating of solid dosage forms. *Pharm Res* 11(6) (1994) 882-8.
- [11] Galdeano MC, Wilhelm AE, Mali S, Grossmann MVE. Influence of thickness on properties of plasticized oat starch films. *Braz Arch Biol Technol* 2013;56(4):637-44.
- [12] Sharma R, Kamboj S, Singh G, Rana V. Development of aprepitant loaded orally disintegrating films for enhanced pharmacokinetic performance. *Eur J Pharm Sci* 2016;84:55-69.
- [13] Borges JG, Silva AG, Cervi-Bitencourt CM, Vanin FM, Carvalho RA. Lecithin, gelatin and hydrolyzed collagen orally disintegrating films: functional properties. *Int J Biol Macromol* 2016;86:907-16.
- [14] Li Y, Pham JQ, Johnston KP, Green PF. Contact angle of water on polystyrene thin films: Effects of CO<sub>2</sub> environment and film thickness. *Langmuir* 2007;23(19):9785-93.
- [15] Rongthong T, Sungthongjeen S, Siepmann F, Siepmann J, Pongjanyakul T. Quaternary polymethacrylate–magnesium aluminum silicate films: Water uptake kinetics and film permeability. *Int J Pharm* 2015;490(1-2):165-72.
- [16] Zheng W, Sauer D, McGinity JW. Influence of hydroxyethylcellulose on the drug release properties of theophylline pellets coated with Eudragit® RS 30 D. *Eur J Pharm Biopharm* 2005;59(1):147-54.