Regular Article

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Effect of the External Lubrication Method for a Rotary Tablet Press on the Adhesion of the Film Coating Layer

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External lubrication is a useful method which reduces the adhesion of powder to punches and dies by spraying lubricants during the tableting process. However, no information is available on whether the tablets prepared using an external lubrication system can be applicable for a film coating process. In this study, we evaluated the adhesion force of the film coating layer to the surface of tablets prepared using an external lubrication method, compared with those prepared using internal lubrication method. We also evaluated wettability, roughness and lubricant distribution state on the tablet surface before film coating, and investigated the relationship between peeling of the film coating layer and these tablet surface properties. Increasing lubrication through the external lubrication method decreased wettability of the tablet surface. However, no change was observed in the adhesion force of the film coating layer. On the other hand, increasing lubrication through the internal lubrication method, decreased both wettability of the tablet surface and the adhesion force of the film coating layer. The magnesium stearate distribution state on the tablet surface was assessed using an X-ray fluorescent analyzer and lubricant agglomerates were observed in the case of the internal lubrication method. However, the lubricant was uniformly dispersed in the external lubrication samples. These results indicate that the distribution state of the lubricant affects the adhesion force of the film coating layer, and external lubrication maintained sufficient lubricity and adhesion force of the film coating layer with a small amount of lubricant.

Key words external lubrication; adhesion force; tablet surface; film coating layer; magnesium stearate

Lubricants are used as an excipient to prevent the adhesion of powders to punches and dies in the compression process for oral dosage tablet manufacturing, and are usually added at a ratio of 1% or less (0.25–0.5%) in the mixing process.1) In the internal lubrication method, the lubricant is mixed with other raw materials in the mixing process, and then the mixture is compressed using a tableting machine in the compression process. However, in the case that a large amount of a lubricant is needed to prevent adhesion to punches and dies for the characteristics of the drug substance, a delay in disintegration and retarded dissolution may occur.2,3) As the hydrophobic lubricant covers the surface of the tablet, this results in poor wettability and prevents water penetration.4,6)

In the external lubrication method, a lubricant is directly sprayed onto the punches and dies of a tableting machine using a lubricant spray nozzle before the powder is compressed during the compression process, and the lubricant is localized on the surface of the punches and dies.7–11) Therefore, using this method, the adhesion of powder to the punches and dies is reduced using a small amount of lubricant. The lubricant is quantitatively supplied to the lubricant agitator from a lubricant filling hopper using a powder surface sensor, and the agitated lubricant is dispersed using compressed air from the lower part of the pipe, which passes through the air tube, and is sprayed from a nozzle onto the surface of the punch and die. We have already reported that it is important to control the discharged amount of lubricant, the amount of dust-collecting air, and the rotation speed of the tableting machine to control the external lubrication.7,12) It has been reported that the tablets produced through external lubrication have a higher hardness and better disintegration and dissolution properties than those of tablets produced using internal lubrication because of the small amount of lubricant.11,13)

As mentioned above, external lubrication is a useful method to reduce problems during the tableting process and improve the properties of plain tablets. However, if tablets are sensitive to humidity, or have an unfavorable taste or smell, they need to be coated using a film coating.14) Therefore, it is important to evaluate the effect of external lubrication on film coating performance. There are several reports that hydrophobic lubricants have a negative effect on the coating performance of tablets.15–19) These reports explained that lubricant covering the surface of tablets results in a loss of adhesion between the tablet surface and the coating film because of hydrophobic nature of lubricants. Specifically, Pandey et al. reported that the concentration of magnesium stearate (Mg-St) significantly affects the frequency of logo bridging on a coated tablet, which is caused by poor adhesion between the film and tablet substance.19) In addition, it has been reported that the roughness of the tablet surface and the porosity of uncoated tablets affect peeling of the film coating layer from the tablet surface.20) In the case of external lubrication, although the amount of lubricant in the tablet is less than that of internal lubrication, there is potential that the film coating layer may be easily peeled off from the tablet.

The aim of the current study is to assess the influence of...
the external lubrication method on the film coating layer. We evaluated the adhesion force of the film coating layer to the surface of an tablet prepared using the external lubrication method. We also evaluated contact angle as an indicator of wettability, roughness and lubricant distribution state on the tablet surface of an uncoated tablet, and investigated the relationship between peeling of the film coating layer and these tablet surface properties. In addition, we evaluated tablets prepared using internal lubrication, and compared their properties with those of tablets prepared using an external lubricant.

**Experimental**

**Materials** Lactose monohydrate (Dilactose®, R, Freund Corporation, Tokyo, Japan) and microcrystalline cellulose (Ceolus® PH 101, Asahi Kasei Corporation, Tokyo, Japan) were used to manufacture the tablets. The lubricant is Mg-St (general grade, Taihei Chemical Industrial Co., Ltd., Osaka, Japan). Hypromellose (TC-5, Shin-Etsu Chemical Co., Ltd., Tokyo, Japan), yellow ferric oxide (Kishi Kasei Co., Ltd., Tokyo, Japan), iron oxide (Kishi Kasei Co., Ltd.) and titanium oxide (Tipaque A-100, Ishihara Sangyo Kaisha, Ltd., Osaka, Japan) were used for the film coating agent.

**Preparation of Tablet Using the External Lubrication Method** The manufacturing conditions are shown in Table 1. Lactose monohydrate (32.0 kg) and microcrystalline cellulose (8.0 kg) were blended using the tablets. The tablets were prepared using an external lubrication system (EXTALUB, Hata Tekkosho Co., Ltd., Kyoto, Japan) and a rotary tabletting machine (HT-X20, Hata Tekkosho Co., Ltd., Kyoto, Japan). Samples with different amounts of lubricant were prepared using the external lubrication method under the conditions shown in Table 2. The similar range of Mg-St contents with our previous study (0.035–0.147 mg/tab) was selected (previous study: 0.040–0.170 mg/tab), and no significant change had been observed in tablet properties (hardness and disintegration time) with the range of reported conditions. The tablet weight was 180 mg and the tablet thickness was 2.6 mm using a flat punch, with a diameter of 8.5 mm. The coated tablets were prepared using a perforated coating system (HICOATER 30, Freund Corporation, Tokyo, Japan).

**Preparation of Tablets Using the Internal Lubrication Method** Lactose monohydrate, microcrystalline cellulose and Mg-St were blended using a bin blender to prepare the final blend. Mg-St was added at 0.36, 0.5, 1.0, 1.5, 2.0, 3.0 or 5.0% of the total formulation. In order to confirm the effect of the amount of Mg-St on the peeling of film coating layer, and make the difference clear between internal and external method, in addition to 1% or less concentration which is commonly used, more than 1% (up to 5%) were selected as the amount of Mg-St. The tablets and coated tablets were prepared using the same equipment and conditions as with the external lubrication method.

**Measurement of the Contact Angle** In order to evaluate the lubricant performance of the tablet, the contact angle of the core tablet before film coating was measured using the 2θ method with a contact angle meter (Type CA-V, Kyowa Interface Science, Saitama, Japan). The measurement was performed after 100 ms of adding 2 µL drops of purified water to the center of upper surface of the tablet. Five tablets were tested for contact angle.

**Measurement of the Adhesion Force of the Film Coating Layer** The adhesion force of the film coating layer was measured using previously reported methods. The texture analyzer (TA-XT2i, Stable Micro Systems Ltd., London, U.K.) shown in Fig. 1A was used for the measurement of the adhesion force of the film coating layer. As shown in Fig. 1B, a tablet was cut approximately 1 mm along the corners of the back side using a cutter, so that the entire tablet surface was peeled off. A piece of double-sided tape (NW-U 15SF, adhesive force 103 N/25 mm, shear strength adhesive 112 N/cm², Nichiban Co., Ltd., Tokyo, Japan) was attached to the tip of the texture analyzer arm shown in Fig. 1C, and the tablet was set on the table. The tip of the jig with the double-sided tape was pressed against the back side of the tablet and then pulled.

![Image](https://example.com/image.png)
apart, and the force required to peel the coating layer off was measured. 10 tablets were tested for adhesion force.

Measurement of Surface Roughness In order to confirm the condition of the tablet surface with different lubrication conditions, its roughness was measured using a laser microscope (VK-9700, Keyence Corporation, Osaka, Japan), and the measurement range was a 2 mm x 3 mm square in the tablet center, and the roughness criterion was the arithmetic average roughness ($R_a$). The arithmetic average roughness (calculated as $R_a = (\sum_{i=1}^{N} |Z_i - \bar{Z}|)/N$, where $Z_i$ is the individual height value of the measurement point, $\bar{Z}$ is the mean value of all the height data points and $N$ is the number of measurement points) was used as the standard roughness.

Analysis of Mg-St Content Three tablets were disintegrated in approximately 35 mL of 0.1 mol/L nitric acid with ultrasonic irradiation for 10 min or more, and then the sample solution was warmed in a bath at 70–80°C. After cooling at room temperature, the sample was diluted to 50 mL using 0.1 N nitric acid, and the solution was filtered using a 0.45 μm filter. Calibration curves were established by preparing solutions of various magnesium concentrations using a magnesium standard solution (Mg 1000, Kanto Chemical Co., Inc., Tokyo, Japan) and 0.1 mol/L nitric acid. The frame method of an atomic absorption spectrophotometer (Z-2000, Hitachi High-technologies Corporation, Tokyo, Japan) was used for analysis of Mg-St content, and the wavelength was set to 285.2 nm.

The Mg-St concentration in the sample solution was calculated using a calibration curve. The nitric acid solution (0.1 mol/L) was prepared by diluting 60% nitric acid (nitric acid [specific gravity, 1.38], Kanto Chemical Co., Inc.) with distilled water (Wako Pure Chemical Industries, Ltd., Osaka, Japan). A blank solution was prepared from the final blend without Mg-St to determine the baseline response for the test solution.

Mapping of Mg-St Distribution on the Tablet Surface before Film Coating An X-ray fluorescent analyzer (Orbis PC, AMETEK Co., Ltd., Tokyo, Japan) was used for mapping of the Mg-St distribution on the surface of the tablet before film coating. The tube voltage was set at 15 kV, the tube current value was set to 900 μA, and the sample chamber atmosphere was vacuumed. In fluorescence X-ray spectrometry, generated fluorescent X-rays are detected when a sample is irradiated with X-rays, and the type and concentration of the elements contained in the sample can be obtained from the wavelength and intensity of these fluorescent X-rays.

Statistics Statistical analyses were performed using ANOVA with Dunnett’s multiple comparison test, where a probability value of $p < 0.05$ was considered to indicate statistical significance.

Results and Discussion

Wettability and Adhesion Force of the Film Coating Layer The impact of the amount of lubricant used in external lubrication on the tablet surface wettability and the adhesion force of the film coating layer is presented in Fig. 2. The contact angle was selected as an indicator of wettability. The contact angle increased with an increasing amount of Mg-St as the external lubricant (Fig. 2A). In other words, the tablet surface wettability decreased as the amount of Mg-St as the external lubricant increased. This indicates that with an increasing amount of Mg-St as the external lubricant, the area covered by the hydrophobic lubricant was increased. However, contrary to our hypothesis, no change was observed in the adhesion force of the film coating layer when the amount of Mg-St as the external lubricant was increased (Fig. 2B). In our previous study, when the amount of Mg-St in externally lubricated tablet increased, contact angle increased; whereas, significant change was not observed in disintegration time. Adhesion force and disintegration time showed similar tendency to the amount of Mg-St.

The impact of the amount of Mg-St as the internal lubricant on the tablet surface wettability and the adhesion force of the film coating layer are presented in Fig. 3. As with the external lubrication, the contact angle increased with an increasing amount of Mg-St as the internal lubricant (Fig. 3A). However, contrary to the external lubricant, the adhesion force of the film coating layer decreased with an increasing amount of Mg-St as the internal lubricant (Fig. 3B). In particular, when the amount of Mg-St was more than 0.9 mg/tablet, the adhesion force showed a significantly lower value than that of no lubricant. Since it was unclear whether lubricant amounts on the surface of tablets were quantitatively different between internal and external lubrication methods, the Mg-St concentrations at the surface layer of externally lubricated tablets were estimated by the same method in our previous report. As a result, Mg-St concentrations at the surface layer of externally lubricated tablets were estimated to be 0.2–0.8 wt% in this study. In this range, adhesion force was changed from 4704 to 3616 gf. On the other hand, adhesion forces of the internally
lubricated tablets at 0.36, 0.5 and 1.0% in Mg-St concentration were 4038, 3091 and 2724 gf, respectively. It indicated that external lubrication showed higher adhesion force than that of internal lubrication at almost the same Mg-St concentration values considering the concentration of surface of tablet.

Figure 4 shows the relationship between the adhesion force of the film coating layer and the contact angle in samples with different amounts of Mg-St. When the contact angle showed similar values for the two lubrication methods, the adhesion force of the film coating layer of externally lubricated tablets was higher than that of internally lubricated tablets.

**Surface Roughness** Since a correlation between the adhesion force of the film coating layer and the wettability of the tablet surface was not observed with the external lubrication method, we evaluated the surface roughness of the tablets. A comparison of the surface roughness of the internally and externally lubricated tablets is presented in Fig. 5. There was no difference in the roughness of the tablet surface between the internally and externally lubricated tablets, and the change in the amount of the lubricant did not affect the roughness of the tablet surface.

**Mg-St Distribution on the Tablet Surface** The Mg-St distribution state on the tablet surface, assessed using X-ray fluorescent analyzer mapping, is presented in Fig. 6. Using this mapping technique, the distribution state of a specific element can be confirmed. In the case of mapping the tablet surface with respect to magnesium, portions of the tablet with more magnesium are displayed with a brighter color. In each lubrication method, with an increasing amount of Mg-St, the brightness of the tablet surface increased (Fig. 6A). Enlarged mapping results of the central position of the tablet surface are presented in Fig. 6B. The lubricant on the tablet surface was uniformly dispersed with the external lubrication method, whereas lubricant agglomerates were observed with the internal lubrication method and with an increasing amount of Mg-St.

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**Fig. 3.** The Impact of the Amount of Internal Lubricant on: (A) Wetting of the Tablet Surface and (B) the Adhesion Force of the Film Coating Layer

Points represent the average values (±S.D.) obtained from five replicates (A) or ten replicates (B). *p<0.05, **p<0.01 compared with no lubricant.

**Fig. 4.** The Relationship between the Adhesion Force of the Film Coating Layer and the Contact Angle

**Fig. 5.** Comparison of the Surface Roughness of the Internally and Externally Lubricated Tablets
lubricant, the number of agglomerates were increased. Since the external lubrication system employs a mechanism to uniformly spray the lubricant onto the surface of the punch and die using compressed air without agglomeration, agglomerates were not observed on the tablet surface in the case of external lubrication. Therefore, the external lubrication method maintains sufficient lubricity and a sufficient adhesion force of the film coating layer, using a small amount of lubricant. However, in the case of the internal lubricant, a scattering of lubricant agglomerates was observed and the scattered lubricant was considered not to deagglomerate even with a sufficient amount of lubricity, and even when sufficient mixing was performed using the mixing bin blender. The final blend contained lubricant agglomerates which were compressed during the tableting process. Therefore, the agglomerates are thought to remain in the tablet. In fact, Ehara et al. evaluated the surface of internally lubricated tablets using energy–dispersion X-ray analysis, and reported that Mg-St was not distributed uniformly on the tablet surface.23) Therefore, it is likely that the lubricant agglomerates promoted peeling of the film coating layer from the surface of the tablet, and the adhesion force of the film coating layer decreased with an increasing amount of Mg-St when using the internal lubrication method.

Conclusion

In the current study, the peeling of the film coating layer and tablet surface properties were investigated in order to assess the effect of external lubrication on the film coating layer. With an increasing amount of lubrication when using the external lubrication method, the wettability of the tablet surface decreased. However, no change was observed in the adhesion force of the film coating layer. When the amount of lubrication was increased when using the internal lubrication method, both the wettability of the tablet surface and the adhesion force of the film coating layer were decreased. Lubricant agglomerates were observed on the tablet surface in the case of the internal lubrication method. These scattered agglomerates on the tablet surface may cause some peeling of the film coating layer. However, the lubricant on the tablet surface was uniformly dispersed in the case of the external lubrication method. These results indicate that the distribution state of the lubricants on the tablet surface affect the adhesion force of the film coating layer, and external lubrication maintained sufficient lubricity and a sufficient adhesion force of the film coating layer, using a small amount of lubricant. As a result, the excellent lubricity of the external lubrication method not only reduces powder adhesion to the punch and die during the tableting process but also prevents peeling of...
the film coating layer.

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Conflict of Interest The authors declare no conflict of interest.

References