



## Lubrication properties of potential alternative lubricants, glycerin fatty acid esters, to magnesium stearate

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### ABSTRACT

To study the usefulness of glycerin fatty acid ester Poem TR-FB® (TR-FB) and Poem TR-HB® (TR-HB) as lubricants, pressure transmission ratio, ejection force, disintegration time, and tensile strength were measured at different concentrations and mixing times for granules and tablets. When each lubricant was mixed at 0.1–3.0%, the increase in the pressure transmission ratio that was equal to or greater than that of Mg-St as well as the reduction in the ejection force was observed at a low concentration in both TR-FB and TR-HB, proving that they have excellent lubrication performance. The granules that were lubricated with TR-FB and TR-HB at even low concentration of 0.4% showed a more stable and sufficiently lower ejection force than with Mg-St from the first tablet after the start of compression. When they were mixed for 5–60 min, while the mixture with Mg-St showed a low pressure transmission ratio of 82% and a high ejection force of 500 N in the first tablet even when the mixing time was 60 min, a high pressure transmission ratio and a low ejection force were observed in TR-FB and TR-HB from the first tablet after mixing for 5–60 min, and these were maintained thereafter. As for the disintegration time and the tensile strength, a prolonged disintegration time and a decreased tensile strength, which are disadvantages of Mg-St, were not observed in TR-FB and TR-HB. Based on these results, it was concluded that TR-FB and TR-HB are useful as alternative lubricants to Mg-St.

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### 1. Introduction

Magnesium stearate (Mg-St) is widely used as a lubricant in solid pharmaceutical formulations, however also is widely known that, as the concentration in a formulation increases, it will cause manufacturing problems such as reduction in tablet hardness (Strickland et al., 1956), prolonged disintegration time (Strickland et al., 1956; Udeala et al., 1980; Flores et al., 2000; Uğurlu and Turkoğlu, 2008) and retarded dissolution (Levy and Gumtow, 1963; Murthy and Samyn, 1977). Precaution for potential biological contamination is important in the use of excipients of animal origin that includes some of Mg-St brands. In addition, to assure the uniform quality of pharmaceutical products, it is necessary to discard initial tablets after starting compression until the uniform lubrication effect takes place.

In order to overcome these disadvantages of Mg-St, a variety of substances, including hydrophilic organic materials such as sodium stearyl fumarate (Hölzer and Sjögren, 1979; Chowhan

and Chi, 1986), sucrose fatty acid esters (Shibata et al., 2002), glycerin bibehenate (Compritol®) (N'Diaye et al., 2003), magnesium lauryl sulfate (Salpekar and Augsburg, 1974), and hexagonal boron nitride (Uğurlu and Turkoğlu, 2008); hydrophobic organic materials; and inorganic materials, have been evaluated so far as alternative lubricants to Mg-St. In addition, the effect of cotreatment with proper lubricant and Mg-St on the lubrication properties has also been evaluated (Wang and Chowhan, 1990; Adeagbo and Alebiowu, 2008). Although they have about the same lubricating effects as Mg-St, the concentration in which they exert lubricating effects are 2.0% for sucrose fatty acid esters and 0.5–1.0% for hexagonal boron nitride indicating that it is necessary to add an equal or greater amount than Mg-St.

As for alternative lubricants to Mg-St, we focused on 2 types of glycerin fatty acid esters (Poem TR-FB® (TR-FB) and Poem TR-HB® (TR-HB)) and have examined their usefulness as lubricants (Aoshima et al., 2005). Interestingly, when they were mixed at 0.5–3.0%, it was found that: at 0.5%, both the pressure transmission ratio and the ejection force were equal to those of Mg-St; even if the concentration or mixing time was increased, the disintegration time was not prolonged and no reduction in the tablet hardness was observed. However, to prove the usefulness of TR-FB and TR-HB as alternative lubricants to Mg-St or other lubricants, it is necessary to

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**Table 1**  
Physical properties of lubricants and granules.

|          | Particle size distribution ( $\mu\text{m}$ ) |      |      | Specific surface area ( $\text{m}^2/\text{ml}$ ) |
|----------|----------------------------------------------|------|------|--------------------------------------------------|
|          | D10                                          | D50  | D90  |                                                  |
| Mg-St    | 3.5                                          | 11.4 | 31.4 | –                                                |
| TR-FB    | 1.6                                          | 3.8  | 12.7 | 1.9                                              |
| TR-HB    | 2.4                                          | 8.5  | 20.5 | 1.1                                              |
| Granules | 595                                          | 650  | 700  | –                                                |

The data are the average values of three or five runs. –; not determined.

determine whether TR-FB and TR-HB could exert their lubrication effects at the low concentrations of less than 0.5%, and to evaluate the initial lubrication properties of TR-FB and TR-HB when their concentrations and mixing times are changed. In addition, it would be critical to clarify the lubrication mechanism of TR-FB and TR-HB for using them in a manufacturing process.

In this study, we measured the pressure transmission ratio and the ejection force, as lubricant properties, not only at the initial phase of the compression but also at the steady-state phase of the compression. Besides, we also measured the disintegration time and the tensile strength of tablets, as tablet characteristics, at the steady-state phase of the compression.

## 2. Materials and methods

### 2.1. Materials

Magnesium stearate (vegetable origin, specifications as a drug additive, listed in the Japanese Pharmacopoeia Fourteenth Edition (JP15), abbreviated as Mg-St) was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). Triglycerin full behenate (Poem TR-FB<sup>®</sup>, vegetable origin, specifications as a food additive, referred to as TR-FB), and triglycerin half behenate (Poem TR-HB<sup>®</sup>, vegetable origin, specifications as a food additive, referred to as TR-HB) were kindly provided by Riken Vitamin Co., Ltd. (Tokyo, Japan). The median diameter (D50%) of Mg-St, TR-FB, or TR-HB was 11.4, 3.8 and 8.5  $\mu\text{m}$ , respectively, measured by a laser diffraction method (LS 13 320, Beckman Coulter (Tokyo, Japan) for Mg-St, Microtrac<sup>®</sup> MT-3000, Nikkiso Co. Ltd. (Tokyo, Japan) for TR-FB and TR-HB). Specific surface area of TR-FB or TR-HB was 1.9, and 1.1  $\text{m}^2/\text{ml}$ , respectively. These parameters are listed in Table 1. Chemical structure and other physicochemical properties such as melting point and moisture content have already been reported in our previous paper (Aoshima et al., 2005).

Lactose monohydrate, listed in JP15 (DMV INTERNATIONAL Co., Ltd.) and corn starch, listed in JP15 (Nihon Shokuhin Kakou Co., Ltd.) were used as fillers, and solid-state hydroxypropylcellulose, listed in JP15 (HPC-L<sup>®</sup>, Nippon Soda Co., Ltd.) was used as a binder.

### 2.2. Granulation

In the present study, wet granulation was chosen for granulation blend, because the granule formulation is most popular in tableting, and it constitutes only two components such as granules and lubricants, and it is easy to determine the effects of lubricants. Using a mixer (Fuji Medical Equipment Co. Ltd.), 350 g of lactose monohydrate and 150 g of corn starch were mixed for 10 min. The ratio of lactose monohydrate and corn starch was referred to the standard formulation given by the Society of Powder Technology, Japan/Division of Particulate Design and Preparations. A total of 100 g of 5.0% water solution of HPC-L was added to this powder by spraying, and the mixture was subsequently kneaded for 10 min. Granulation was performed using a rotating squeeze type granulator with a sieve size of 0.8 mm (Hata Iron Work Co. Ltd.). The granules were dried using an oven at 50 °C for 12 h or longer. The

moisture content of the granules was 0.95%. After drying, they were sieved through a 1680  $\mu\text{m}$  sieve and the granules that did not pass through a 350  $\mu\text{m}$  sieve were collected. This process was repeated several times, and the resultant granules were then mixed uniformly and subjected to the experiments. The median diameter (D50%) of granules was 650  $\mu\text{m}$ . D10% and D90% of granules were 595 and 700  $\mu\text{m}$ , respectively, measured according to the JP15 sieved method (Tsutsui Rikagaku Kikai Co., Ltd., Japan). These properties have been listed in Table 1.

### 2.3. Tablet preparation and determination of the pressure transmission ratio and the ejection force

One hundred and fifty (150)g of the granules were fed in a V-shaped mixer (Microtype Transparent Mixer S-3, Tsutsui Rikagaku Kikai Co., Ltd.) and flattened on its surface. After flattening, Mg-St, TR-FB, or TR-HB was added to the center of the granules and was mixed at a rotation rate of 35 rpm for 5 min. In previous works, when Mg-St was mixed with the granules at the concentrations of 3.0, 4.0, 5.0 and 6.0%, the pressure transmission ratios showed a plateau (unpublished). Therefore, the lubricant concentrations of 0.1, 0.2, 0.3, 0.4, 0.5, 1.0, 2.0, and 3.0% were selected in the present study. The tablets were prepared using a single punch tablet machine (N20-E, Okada Seiko Co. Ltd.) with diameter of 8 mm (flat-faced punch) and each tablet weight was 200 mg. The tableting speed was 10 tablets per minute and the tableting force was 10 kN. Mixing times of the lubricants with granules were 5, 15, 30 or 60 min. The concentration of each lubricant was fixed at 0.5%, and the applied tableting force was 10 kN. The pressure of the punch during tableting was measured using a load cell with a mobile type data recorder (NR-1000, Keyence), and it was converted to the force applied to the die. The pressure transmission ratio ( $P_r$ ) was calculated by the following formula:

$$P_r = \frac{P_l}{P_u} \times 100,$$

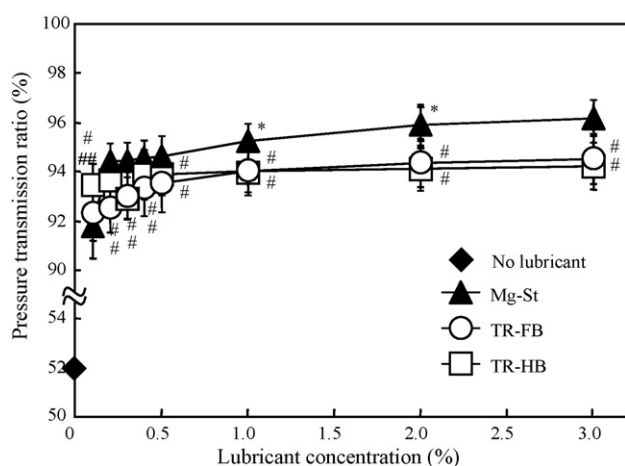
where  $P_l$  is the maximum pressure of the lower punch and  $P_u$  is the maximum pressure of the upper punch in the tableting process.

The ejection force i.e., the force applied to the lower punch during tablet ejection, was measured by a 2 kN load cell as described above.

### 2.4. Determination of tablet disintegration time and tensile strength

Tablets subjected to the test were prepared as described in Section 2.3. To determine the effects of the lubricant concentration and mixing time on the disintegration time, the lubricant concentrations were used for 0.1, 0.2, 0.3, 0.4, 0.5, 1.0, 2.0, and 3.0%, and the mixing times of the lubricants with granules were used for 2, 5, 15 and 30 min. The tableting force applied was 10 kN. Six tablets were selected at random from the tablets prepared, and the disintegration tests were performed according to the JP15 disintegration test using a disintegration tester (Miyamoto Riken Ind. Co. Ltd.). Distilled water at 37  $\pm$  0.5 °C was used as the test fluid.

For the tensile strength measurements, 10 tablets were selected at random. The tensile strength of tablets was determined by diametrical compression tests, which were performed by a hardness meter with a 300 N load cell (precision of 1 N, PC-30, OKADA SEIKO Co., Ltd., Japan) in order to accurately measure the maximal diametrical crushing force ( $F$ ). Besides, the diameter and the thickness of tablets were measured using a micrometer with a precision of 0.01 mm (500-302 CD-20, Mitutoyo Corporation, Japan). The tensile strength ( $\sigma$ ) was calculated by the following formula (Fell and



**Fig. 1.** The effect of the lubricant concentration on the pressure transmission ratio. Each point represents an average value obtained from forty determinations ( $\pm$ S.D.). \* $p < 0.01$ , compared with 0.5% of Mg-St group. \*\* $p < 0.05$ , # $p < 0.01$ , compared with Mg-St group.

Newton, 1970);

$$\sigma = \frac{2F}{\pi Dt},$$

where  $D$  and  $t$  are the diameter and the thickness of tablets, respectively.

### 2.5. Evaluation of the particle sizes of granules after being mixed until 60 min

One hundred and fifty (150) g of the granules and 0.5% TR-HB were mixed with a V-shaped mixer at a rotation rate of 35 rpm for 60 min. At 5, 15, 30 and 60 min after mixing, approximately 450 particles were selected at random from the mixtures. Heywood diameter ( $d$ ) was determined using a software (Win ROOF, MITANI CORPORATION, Japan), by calculating the diameter of circle whose area was equivalent to the actual projected area  $A$  of a particle, as shown by following equation.

$$d = \left( \frac{4A}{\pi} \right)^{1/2}$$

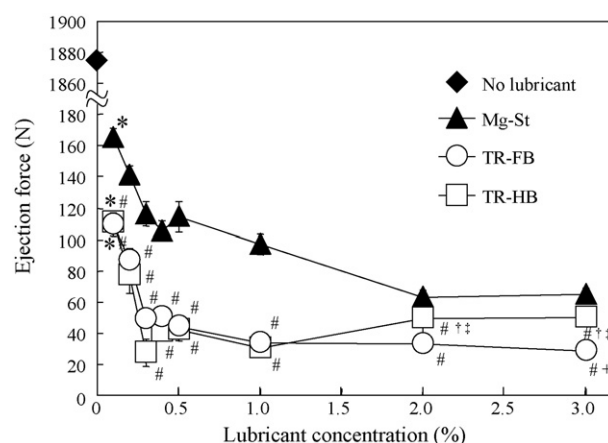
### 2.6. Statistical analysis

Statistical analyses were performed using the ANOVA test. A probability value of  $p < 0.05$  was considered to indicate statistical significance.

## 3. Results and discussion

### 3.1. Effects of the lubricant concentration at the steady-state phase of the compression

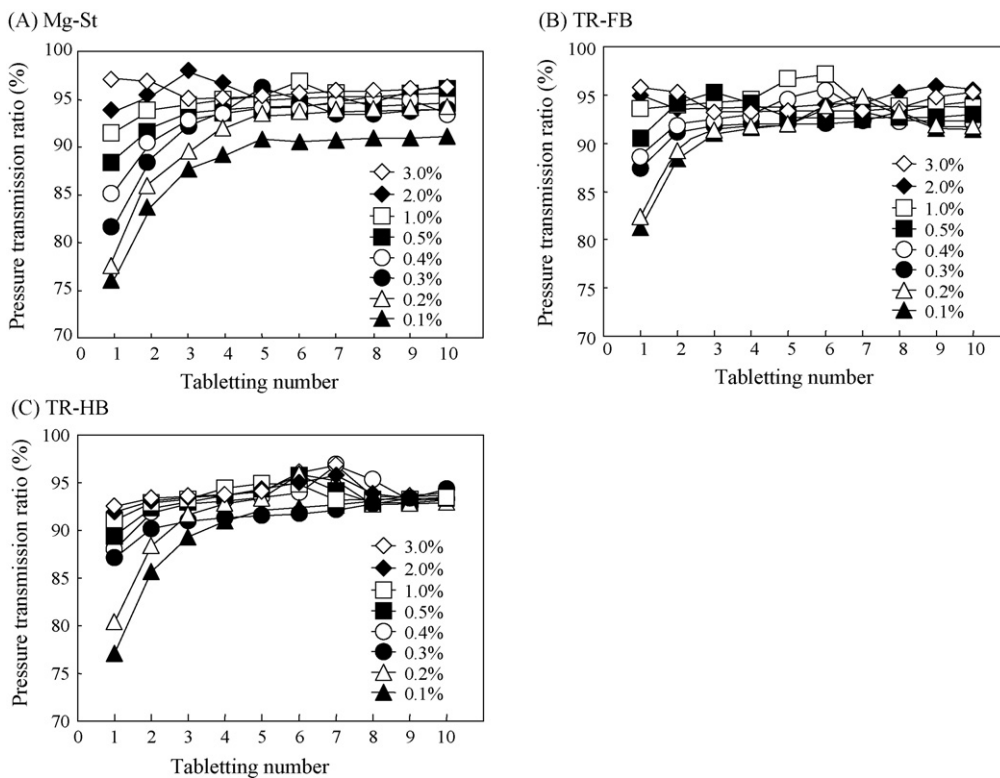
The relationship between the concentration and pressure transmission ratio of each lubricant is shown in Fig. 1. In order to observe steady lubricating properties in each experiment, the data of 10 tablets from the initial phase of compression were not included in this figure. When granules without lubricant were compressed, the average of pressure transmission ratio was 52%. It was shown that, when Mg-St was mixed to those granules at a concentration of 0.1%, the pressure transmission ratio was 91.8%. As the concentration increased, the pressure transmission ratio also gradually increased among 0.5–2.0% ( $p < 0.01$ ), and the pressure transmission ratio reached the maximal value, 96.2%, at a concentration of 3.0%.



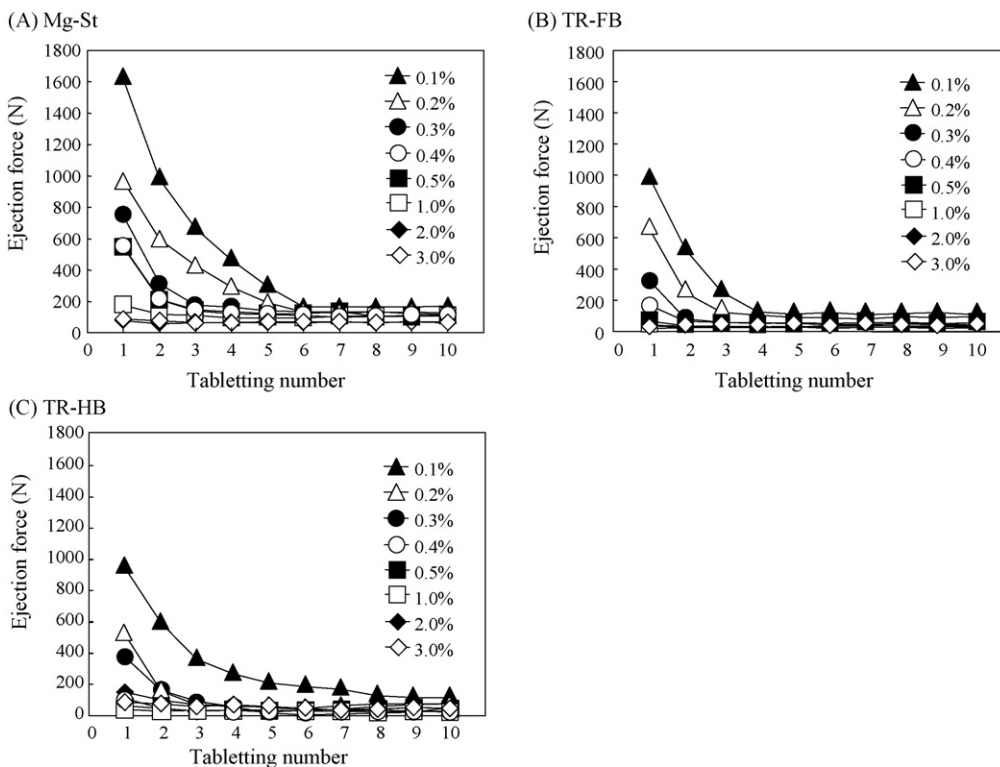
**Fig. 2.** The effect of the lubricant concentration on the ejection force. Each point represents an average value obtained from forty determinations ( $\pm$ S.D.). \* $p < 0.01$ , compared with no lubricant. # $p < 0.01$ , compared with Mg-St group. \* $p < 0.01$ , compared with 2.0% of TR-FB group. † $p < 0.01$ , compared with 1.0% of TR-HB group. ‡ $p < 0.01$ , compared with TR-FB group.

In TR-FB and TR-HB, the pressure transmission ratios at a concentration of 0.1% were 92.3 and 93.5%, respectively, indicating values were significantly higher than that of Mg-St at the same concentration ( $p < 0.05$  for TR-FB,  $p < 0.01$  for TR-HB). Thereafter, as the concentration increased, the pressure transmission ratio slightly increased (not significant versus that of 0.1% TR-FB and TR-HB), and the pressure transmission ratio reached the maximum values, 94.5 and 94.3%, respectively, at a concentration of 3.0%. At concentrations higher than 0.2%, Mg-St showed a significant higher pressure transmission ratio than those of TR-FB and TR-HB ( $p < 0.01$ ). While there are slight differences at higher concentrations, it is practically concluded that there is not a considerable difference in the lubricant performance among those lubricants.

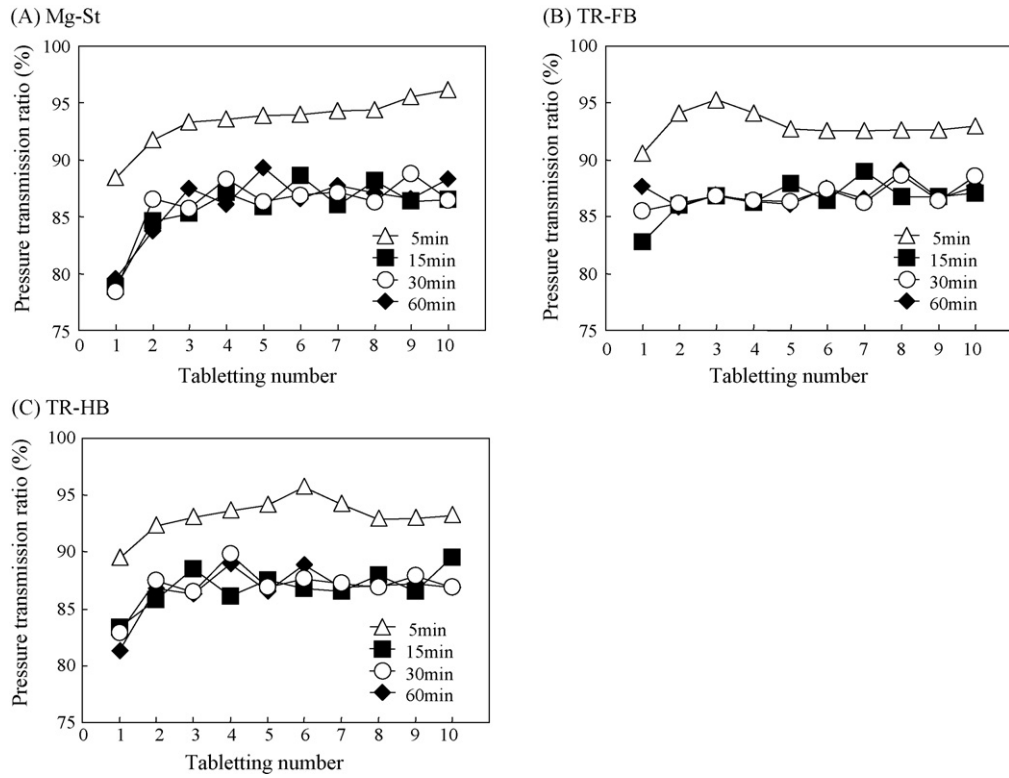
The relationship between the concentration and the ejection force of each lubricant is shown in Fig. 2. As well as Fig. 1, the data of 10 tablets from the initial phase of compression were also not included in this figure in order to observe steady lubricating properties in each experiment. When granules without lubricant were compressed, the average of ejection force was 1875 N, and tableting problems such as capping and lamination occurred. By addition of 0.1% of Mg-St, TR-FB, or TR-HB, the ejection force was significantly reduced ( $p < 0.01$  versus that without lubricant). When Mg-St was mixed, the ejection force at concentration of 0.1% was 164 N, and, it gradually decreased until the concentration reached 2.0%; then from 2.0 to 3.0%, it was 63 N. With TR-FB or TR-HB, the ejection force was significantly lower than that of Mg-St at all concentrations (0.1%: 108 N, and 1.0%: 30 N,  $p < 0.01$ ). Therefore, these data demonstrated the possibility that TR-FB and TR-HB will supply some advantage on tablet characteristics compared with that of Mg-St. After they were mixed at concentrations of 2.0% and higher, the ejection force of TR-FB significantly decreased ( $p < 0.01$  versus that of 2.0% TR-FB), while the ejection force of TR-HB significantly increased ( $p < 0.01$  versus that of 1.0% TR-HB), and significant differences were observed between TR-FB and TR-HB ( $p < 0.01$ ). Although it is difficult to explain the differences of TR-FB and TR-HB, because various factors were involved in this phenomena, further study for determining the stress relaxation (Ebba et al., 2001), residual die wall force (Takeuchi et al., 2004), and Young's modulus (Ebba et al., 2001) will help for us to make clear the mechanism why the ejection force increased above 2% for TR-HB. Shibata et al. (2002) reported that behenyl acid, which has 22 carbons in its molecule, showed a lower ejection force than Mg-St, which has 18 carbons in its molecule, thus indicating that a lubricant with longer carbon chains showed a higher lubricity than that with lower carbon



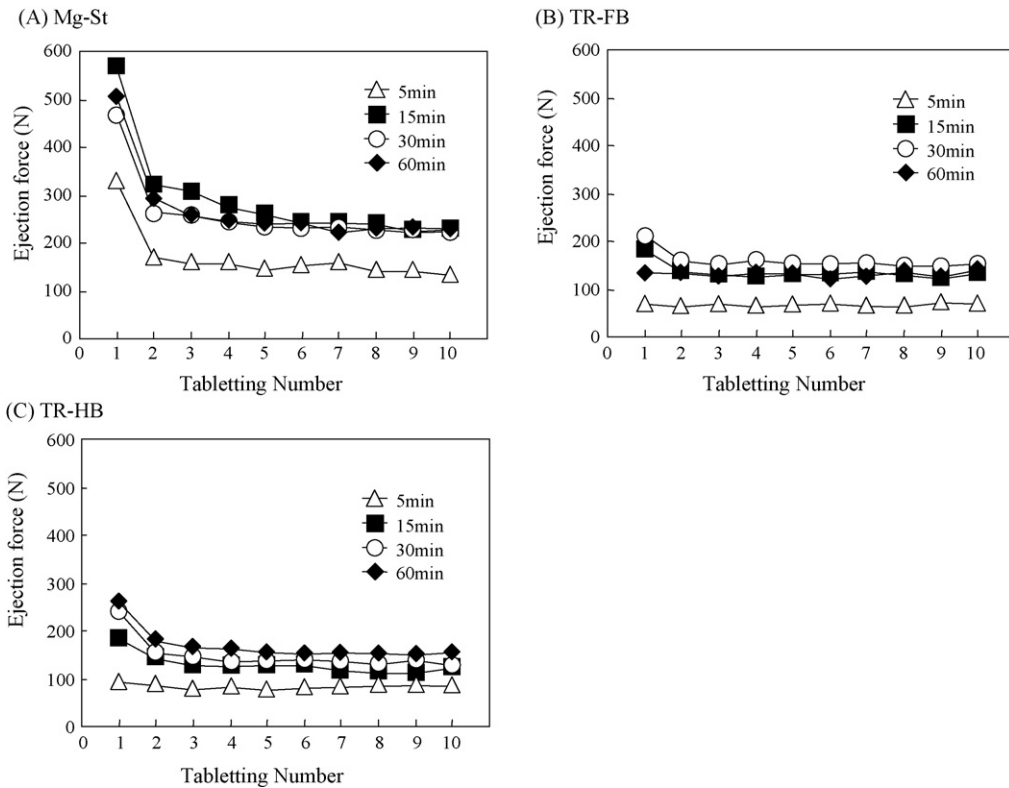
**Fig. 3.** The effect of the lubricant concentrations on the pressure transmission ratio from the start of compression. The lubricant concentration ranges from 0.1 to 3.0%. Each figure represents (A) Mg-St, (B) TR-FB, and (C) TR-HB.



**Fig. 4.** The effect of the lubricant concentrations on the ejection force from the start of compression. The lubricant concentration ranges from 0.1 to 3.0%. Each figure represents (A) Mg-St, (B) TR-FB, and (C) TR-HB.



**Fig. 5.** The effect of mixing times of lubricants on the pressure transmission ratio from the start of compression. The mixing time ranges from 5 to 60 min. Each figure represents (A) Mg-St, (B) TR-FB, and (C) TR-HB.



**Fig. 6.** The effect of mixing times of lubricants on the ejection force from the start of compression. The mixing time ranges from 5 to 60 min. Each figure represents (A) Mg-St, (B) TR-FB, and (C) TR-HB.

chains. In addition, Strickland et al. (1960) also reported that the longer carbon chains might serve as satisfactory tablet lubricants. Our study supported these assumptions by determination of lower ejection forces of TR-FB and TR-HB that have longer carbon chains than Mg-St.

### 3.2. Effects of the lubricant concentration at the initial phase of the compression

Changes in the pressure transmission ratio at the initial phase of the compression up to the 10th tablet are shown in Fig. 3, and changes in the ejection force are shown in Fig. 4. While, for Mg-St, the pressure transmission ratio was constant from the 5th tablet after the start of compression and showed 90–95% at every concentration between 0.1 and 0.5% (Fig. 3A), constant values in the pressure transmission ratio were observed from the 3rd tablet after the start of compression for TR-FB (Fig. 3B), and from the 4th tablet for TR-HB (Fig. 3C). As for the ejection force, until the stabilized ratio values were obtained, Mg-St required the compression of 6 tablets at low concentrations of 0.1–0.2%, and the compression of 3–4 tablets at concentrations of 0.3–1.0%. At high concentrations of 2.0% and higher, stabilized ejection force was obtained from the first tablet after the start of compression (Fig. 4A). On the other hand, for TR-FB and TR-HB, stabilized low ejection force was obtained for 2–4 tablets, even at low concentrations of 0.1–0.4%, and when they were mixed at concentrations of 0.5% and higher, stabilized low ejection force was obtained from the first tablet after the start of compression (Fig. 4B and C). The low pressure transmission ratio and high ejection force at the initial phase of compression may be explained by insufficient mixing of the lubricant and granules. However, since these parameters of TR-FB and TR-HB were superior to that of Mg-St, it is speculated that TR-FB and TR-HB are able to easily spread over the surface of granules compared with Mg-St. In addition, Mg-St is generally mixed at 0.5% during the manufacturing process. Therefore, it was proven that, when they were mixed at the same concentration of 0.5%, TR-FB and TR-HB have apparently better lubricant performance than that of Mg-St. Furthermore, it was verified that TR-FB and TR-HB show equal initial lubricant performance when they are mixed at concentrations below 0.5%.

Thus, since both TR-FB and TR-HB showed good lubricant performance from the first compressed tablet, it was suggested that, using TR-FB and TR-HB as a lubricant, products with uniform quality could be produced immediately after the initiation of tablet compression.

### 3.3. Effects of the mixing time of lubricants at the initial phase of the compression

In addition to changes in the concentration, the lubricant properties of Mg-St are affected by the mixing time period. We studied the impact of the mixing time period on the pressure transmission ratio and ejection force for tablets. Mg-St, TR-FB, or TR-HB was mixed to the granules at a concentration of 0.5%, mixed for 5–60 min, and compressed at a compression pressure of 10 kN (Figs. 5 and 6). We expected that lubricants would be distributed more uniformly among the granules over time, and a steady transmission ratio and ejection force would be observed from the first tablet because of the prolonged mixing time. However, even when the mixing time was prolonged until 60 min, Mg-St showed a low pressure transmission ratio of 82% and a high ejection force of 500 N at the 1st tablet (Figs. 5A and 6A).

For TR-FB and TR-HB, the first tablet showed a high pressure transmission ratio and a low ejection force after 5 min of mixing, and these were maintained thereafter (Figs. 5B, C, 6B and C). However, due to the prolonged mixing time, decreasing tendency of the pressure transmission ratio was observed for all lubricants, though

**Table 2**  
Particle sizes of granules after being mixed until 60 min.

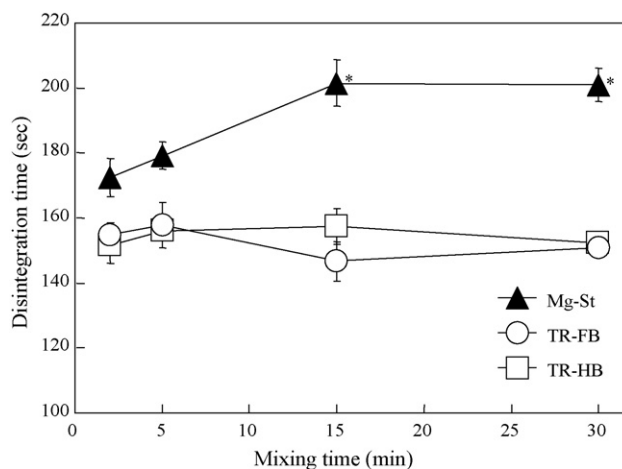
|                                    | Mixing time (min) |                |                |                |               |
|------------------------------------|-------------------|----------------|----------------|----------------|---------------|
|                                    | 0                 | 5              | 15             | 30             | 60            |
| Heywood diameter ( $\mu\text{m}$ ) | 1390 $\pm$ 432    | 1354 $\pm$ 386 | 1181 $\pm$ 394 | 1074 $\pm$ 282 | 938 $\pm$ 192 |

the values of TR-FB and TR-HB are higher than that of Mg-St. In addition, the ejection force in the initial compression phase slightly increased, and followed by stable low ejection force after several tablets were compressed. Lubricants can be uniformly distributed in bulk powders by mixing for a proper period of time, but when being mixed too long, segregation occurs and uniformity decreases; segregation tends to occur particularly when mixing powders containing different particle diameters or different densities such as between the granules and the lubricant.

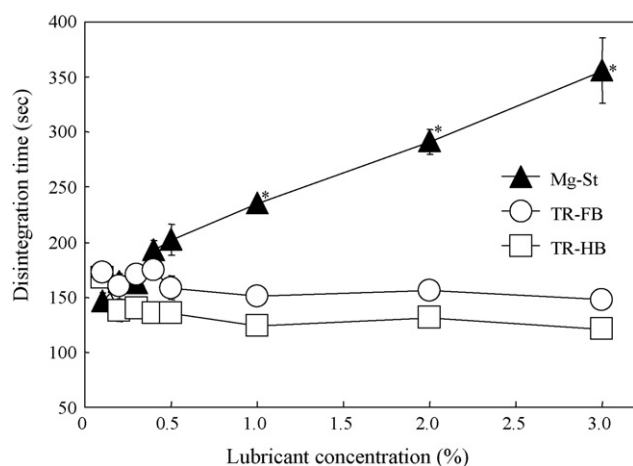
In addition, we also speculated that when being mixed too long, granules were broken, and consequently specific surface area, which is able to contact with Mg-St, of granules increased. Accordingly, we performed additional experiments to evaluate the particle sizes of 150 g granules after being mixed until 60 min (Table 2). As a result, when mixed for 5 min, the particle size of granules was 1354  $\pm$  386  $\mu\text{m}$ , which was equivalent to the size of the untreated granules (1390  $\pm$  432  $\mu\text{m}$ ). However, when mixed for 15, 30 and 60 min, the particle sizes of granules were 1181  $\pm$  394, 1074  $\pm$  282, and 938  $\pm$  192  $\mu\text{m}$ , respectively, suggesting that, in this study, the particle sizes decreased as the mixing time increased, but there were no significant differences among the granules mixed for 15, 30 and 60 min. Therefore, slight decreases of pressure transmission ratio (Fig. 5) and the slight increases of ejection force (Fig. 6) at mixing time from 15 to 60 min might probably be observed. But their functionality of lubricant characteristics still worked on the surface of the granules, the tendencies of stable high pressure transmission ratio and low ejection force might be observed.

### 3.4. Effects of the mixing time and concentration of lubricants on disintegration time of tables

Fig. 7 shows the tablet disintegration time versus the mixing time. While the tablets were disintegrated within 180 s after mixing with Mg-St for 5 min, it took 201 s after mixing for 15 min, and the disintegration time was significantly prolonged ( $p < 0.01$  versus



**Fig. 7.** The effect of mixing times of the lubricants on the disintegration. Each point represents an average value obtained from six determinations ( $\pm$ S.D.). \* $p < 0.01$ , compared with 5 min of Mg-St group.



**Fig. 8.** The effect of lubricant concentrations on the disintegration. Each point represents an average value obtained from six determinations ( $\pm$ S.D.). \* $p < 0.01$ , compared with 0.5% of Mg-St group.

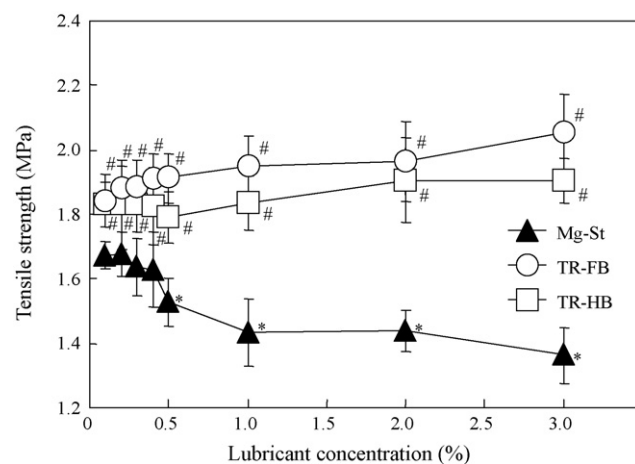
that of Mg-St at 5 min). On the other hand, disintegration time was not prolonged for either TR-FB or TR-HB, even when the mixing time was prolonged.

Fig. 8 shows the tablet disintegration time versus the lubricant concentration. When Mg-St was mixed to granules at a concentration 0.1–0.5%, the disintegration times were 146–201 s. As the concentration was increased, the disintegration time was significantly prolonged ( $p < 0.01$  versus that at 0.5% Mg-St), and the disintegration time at concentrations of 1.0, 2.0 and 3.0% was 235, 290 and 355 s, respectively. On the other hand, in TR-FB and TR-HB, even if the concentration was increased, the disintegration time was not prolonged. The disintegration times at concentrations of 0.1–3.0% were 150–172 s for TR-FB and 120–167 s for TR-HB, respectively, and these results coincided with the data previously reported by Aoshima et al.

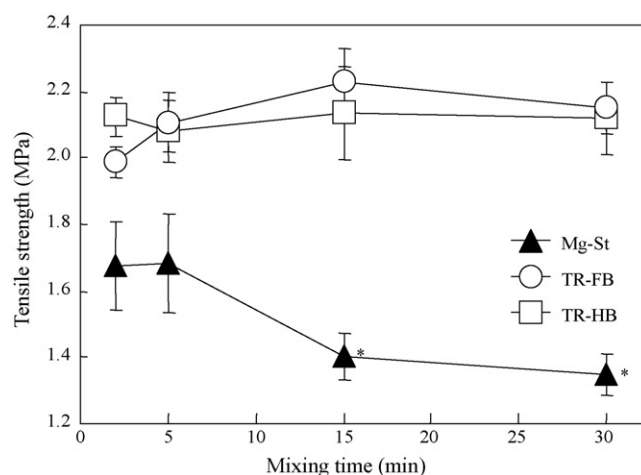
Generally, Mg-St has high water repellency, and increasing the concentration and/or prolonging the mixing time of Mg-St make it possible for a hydrophobic film to form on the particle surface and tablet surface, and the disintegration time is prolonged accordingly (Shah and Mlodozieniec, 1977; Ragnarsson et al., 1979; Bolhuis et al., 1981). Based on this report, we have assumed that TR-FB and TR-HB have low water repellency compared to Mg-St; the possibility of having a different distribution status of lubricant inside the tablet; and no hydrophobic film was observed to form on the particle surface or tablet surface.

### 3.5. Effects of the mixing time and concentration of lubricants on tensile strength of tablets

Figs. 9 and 10 show effects of the lubricant concentration and mixing time on the tensile strength of tablets at the steady-state of the compression. The tensile strength in Mg-St was 1.63–1.68 MPa at concentration from 0.1 to 0.4% (Fig. 9). As the concentration was increased, the tensile strength was gradually decreased ( $p < 0.01$  versus that at 0.4% of Mg-St), and the value at concentration of 0.5, 1.0, 2.0 and 3.0% was 1.53, 1.43, 1.44 and 1.36 MPa, respectively. On the other hand, in TR-FB and TR-HB, the tensile strength at concentration from 0.1 to 0.4% was 1.84–1.91 MPa for TR-FB and 1.82–1.83 MPa for TR-HB, respectively. Interestingly, as the concentration increased from 0.5 to 3.0%, any changes were not observed in the tensile strength for TR-FB and TR-HB, and the values of tensile strength at 0.5, 1.0, 2.0 and 3.0% were 1.91, 1.95, 1.96 and 2.05 MPa for TR-FB and 1.79, 1.83, 1.91 and 1.90 MPa for TR-HB. In addition, it was found that the tensile strength for TR-FB or TR-HB



**Fig. 9.** The effect of lubricant concentration on the tensile strength. Each point represents an average value obtained from ten determinations ( $\pm$ S.D.). \* $p < 0.01$ , compared with 0.4% of Mg-St group. # $p < 0.01$ , compared with Mg-St group.



**Fig. 10.** The effect of mixing time of the lubricants on the tensile strength. Each point represents an average value obtained from ten determinations ( $\pm$ S.D.). \* $p < 0.01$ , compared with 5 min of Mg-St group.

was significantly higher than that of Mg-St at every concentrations ( $p < 0.01$ ).

Furthermore, in Fig. 10, when the mixing time was prolonged to 2, 5, 15 and 30 min, the tensile strength in Mg-St were decreased to 1.67, 1.68, 1.40 and 1.34 MPa, respectively, and significant differences were observed in that mixed with 15 and 30 min ( $p < 0.01$  versus that with 5 min of Mg-St). On the other hand, in TR-FB and TR-HB, even if the mixing time was prolonged, the tensile strength was not changed, and the values at 2, 5, 15 and 30 min were 1.99, 2.01, 2.23, and 2.15 MPa for TR-FB, and 2.12, 2.08, 2.14, and 2.12 MPa for TR-HB. Therefore, these results demonstrated that TR-FB and TR-HB have better tableting performance than that of Mg-St.

## 4. Conclusions

Traditionally, Mg-St has been widely used as an inexpensive lubricant having excellent lubrication effects, but it also has disadvantages such as a reduction in tablet hardness and prolonged disintegration time. In this study, we focused on glycerin fatty acid ester TR-FB and TR-HB as potential alternative lubricants to Mg-St. Their lubricating properties were examined as well as tablet properties in comparison to those of Mg-St. For all of Mg-St, TR-

FB, and TR-HB, the pressure transmission ratio was significantly improved at a concentration of 0.5% and the ejection force prominently decreased for all of them; especially for the ejection force of TR-FB and TR-HB, a value lower than that of Mg-St was observed. For the ejection force of the initial compression, TR-FB and TR-HB were thus both indicated to exert the same effects as the traditional formulation of 0.5% Mg-St at a concentration of 0.2%, and a low ejection force was also observed from the first compressed tablet when TR-FB and TR-HB were mixed at 0.5%. Furthermore, when the mixing time was prolonged until 60 min, a stable low ejection force and a high pressure transmission ratio were observed for both TR-FB and TR-HB immediately at the initial phase of the compression. Moreover, even when the mixing time was longer, disintegration time was not prolonged for either TR-FB or TR-HB. Therefore (although further studies for tablet characteristics such as tablet weight, hardness and disintegration time at the initial phase of the compression would be required to determine how much tablets should be discarded) it is believed that it would be possible to produce products with uniform quality immediately after the start of compression, to control the occurrence of compression loss, and to relieve the load on the tablet machine. Based on these results, it has been concluded that TR-FB and TR-HB are thus useful as alternative lubricants to Mg-St.

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