Mechanical Stress Simulation of Scored Tablets Based on the Finite Element Method and Experimental Verification

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Scored tablets can be divided into equal halves for individual treatment of patients. However, the relationships between scored shapes and tablet characteristics such as the dividing strength, halving equality, and breaking strength are poorly understood. The purpose of this study was to simulate the mechanical stress distribution of scored tablets by using the finite element method (FEM). A runnel of triangle pole on the top surface of flat tablets was fabricated as the score shape. The depth and angle of the scores were selected as design variables. Elastic parameters such as a Young’s modulus and a Poisson ratio for the model powder bed were measured. FEM simulation was then applied to the scored tablets, represented as a continuum elastic model. Stress distributions in the inner structure of the tablets were simulated after applying external force. The adequacy of the simulation was evaluated in experiments using scored tablets. As a result, we observed a relatively good agreement between the FEM simulation and the experiments, suggesting that FEM simulation is advantageous for designing scored tablets.

Key words scored tablet; mechanical stress; simulation; mathematical model; elastic model; finite element method

Tables are the most common solid dosage forms compared to other forms such as powders, granules, and capsules. For the individual treatment of patients, tablets are often divided, and thus, well-designed scored tablets are required for clinical use. van Santen et al.1) reviewed the advantages, limitations, and performance indicators of the score line on tablets; they reported that for many patients, scored tablets are broken unequally and with difficulty, reducing the compliance and reliance on drug therapy. However, Rodenhuis et al.2) surveyed the use of scored tablets as a dosage form and found that scored tablets play an important role in patient treatment. Even when lower-dose tablets are available, patients continue to subdivide tablets for ease of swallowing and adapting the dose. The score shapes may have a large influence on the essential characteristics of tablets, such as the dividing strength, halving equality, and breaking strength. Score shapes are typically determined empirically, but they have not always been reasonably designed. Sovány et al.3) reported that the halving property of scored tablets is affected by tableting machines. Podeczeck et al.4) simulated the influence of the breaking line position of scored tablets on tensile failure by using a finite element method (FEM). They demonstrated that the position of the breaking line significantly affected the breaking strength of scored tablets. Although numerous FEM simulation studies evaluating the powder compaction and mechanical strength of tablets have been reported,5–17) very little is known regarding the mechanical adequacy of score shapes involving dividing strength, halving equality, and breaking strength. The aim of this study was to clarify the effect of score shapes on the essential characteristics of tablets by using FEM simulation. A runnel of triangle pole on the top surface of flat tablets was fabricated as the score shape. The depth and angle of scores were changed as design variables. Other factors such as the tablet shape, thickness, and density may affect the dividing strength, halving equality, and breaking strength. However, we only focused on the depth and angle of scores in this study as the starting point for the potential use of FEM simulation for the design of scored tablets.

Stress distributions on the tablet surfaces were simulated after applying an external force. The bending force and diametrical compression were applied to the various types of scored tablets. The adequacy of FEM simulation was evaluated using scored tablets composed of lactose (LAC) and cornstarch (CS) as diluents, microcrystalline cellulose (MCC) as a binder, and low-substituted hydroxypropyl cellulose (L-HPC) as a disintegrant.

Experimental

Materials Lactose (LAC; Tablettose 80) was purchased from Meggle Japan Co., Ltd. (Tokyo, Japan). Cornstarch (CS; Graflow M) was purchased from Nippon Starch Chemical Co., Ltd. (Osaka, Japan). Microcrystalline cellulose (MCC; Celulose PH-101) was purchased from Asahi Kasei Chemicals Co., Ltd. (Tokyo, Japan). Low-substituted hydroxypropyl cellulose (L-HPC; LH-21) was a gift from Shin-etsu Chemical Co., Ltd. (Tokyo, Japan). Magnesium stearate (Mg-St) was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).

Preparation of Scored Tablets Figure 1 shows a schematic representation of the model scored tablets. Twelve types of scores were fabricated on flat-faced tablets by changing the depth (h=0.50, 0.75, 1.00, 1.50 mm) and angle (θ=45°, 60°, 75°). All ingredients listed in Table 1 were dried at 75°C for 24 h and sieved through a 60-mesh screen. The sieved ingredients were weighed and mixed in a polyethylene bag for 2 min, ex-
cept Mg-St, which was used as a lubricant. Finally, Mg-St was added into the powder mixture and blended for 1 min. Next, 200 mg of the mixed powder was compressed at 4 kN into flat-faced scored tablets, 8 mm in diameter, using a hydraulic press (Model PCH-20, NPa System Co., Ltd., Saitama, Japan).

**Determination of Elastic Parameters** Young’s modulus ($E$) and Poisson rate ($\nu$) were measured as elastic parameters of the tablets. The methods have been fully described in previous reports. Briefly, these parameters were estimated using an instrumented hydraulic press (TK-TB20KN; Tokushu Keisoku Co., Ltd., Yokohama, Japan). The axial upper/lower punch forces and displacements, as well as the radial die-wall pressure, were measured during compaction. Compression and decompression speeds were set at 1 mm/s 350 mg of sample powder was used. The relative packing density at 2 MPa was measured according to the volume of the gap between the upper and lower punches to calculate the initial density of the powder bed.

$E$ and $\nu$ values were determined according to the following equations:

$$E = \frac{9GK}{(3K + G)}$$  \hspace{1cm} (1)

$$\nu = \frac{(3K - 2G)}{2(3K + G)}$$ \hspace{1cm} (2)

where $K$ is the bulk modulus and $G$ is the shear modulus. $K$ and $G$ values were estimated from a stress–strain curve obtained during compression and decompression testing.

**FEM Simulation** In the initial stage of loading the external force onto the tablet, we hypothesized that the tablet represented a continuum elastic model. FEM was applied to estimate the principal stresses generated at the top and lateral surfaces, and along scored lines. To avoid generating a singular point, the shape of the score tip was set to be a fillet surface. The stress distribution was simulated after application of external forces such as bending stress and diametrical compression. The application methods of these external stresses to the scored tablet are illustrated in Figs. 2 and 3. In order to mimic tablet division by hand during the bending simulation, part of the unscored bottom surface of the tablets was fixed at the rigid center line of 0.2 mm wide and 8 mm long (shown as dark gray line), and both ends of the top surface (shown as a dark gray area) were pressurized in the vertical direction at 100 N (Fig. 2). For diametrical compression, the scored tablet was compressed onto a rigid wall by moving the other side horizontally at 100 N (Fig. 3). Stress distributions on the top surface and lateral side contacting the moving wall were estimated by FEM simulation.

**Determination of Tablet Characteristics** As important characteristics of scored tablets, the dividing strength, halving equality, and breaking strength were determined. Figure 4 shows the apparatus for testing the dividing strength. A stainless steel probe with a triangle pole blade (a blade angle of 45° and length of 8 mm) was driven in the vertical direction until the tablets began subdividing. The score line of the tablet was mounted parallel to the direction of the blade length. The maximum force was determined as the dividing strength. The halving equality was gravimetrically evaluated by using the difference factor ($F_{D}$), defined as:

$$F_{D} = \left(\frac{W_A - W_B}{W_A + W_B}\right) \times 100$$ \hspace{1cm} (3)

where $W_A$ and $W_B$ are weights of each halves of the subdivided tablets, respectively. Theoretically, the $F_{D}$ value was expressed as a value 0–100%; a smaller $F_{D}$ value indicates a greater halving equality. The breaking strength of scored tablets was determined using a portable hardness tester (PC-30; Okada Seiko Co., Ltd., Tokyo, Japan). The tablet was mounted on
the hardness tester ensuring that the scored line was placed orthogonally to the direction of diametrical compression.

**Computer Programs** FEM analysis of the tablet properties was performed using ANSYS® version 14.5 (ANSYS Inc., Canonsburg, PA, U.S.A.). Two-way factorial ANOVA and regression analysis were performed using JMP® version 8 (SAS Institute Inc., Cary, NC, U.S.A.).

**Results and Discussion**

**Simulation of Maximum Principal Stress** To perform FEM simulation, the scored tablet was represented as a continuum elastic model. From a stress–strain curve determined using the test formulation listed in Table 1, elastic parameters, \( E = 2.35 \pm 0.07 \text{ GPa} \) and \( \nu = 0.08 \pm 0.01 \) as the mean±standard deviation (S.D.) for three determinations, were estimated, and were used as parameters in the FEM simulation. The principal stresses were given as the stress tensor elements when the shear stress components became zero and were represented as maximum (\( \sigma_1 \)), intermediate (\( \sigma_2 \)), and minimum (\( \sigma_3 \)) principal stresses. In this study, we employed the \( \sigma_1 \) value as a representative of the stress generated after applying the external force to the tablets. When the \( \sigma_1 \) value was positive, the tensile force was working at the relevant site of the tablets and vice versa.

**Effect of Bending Force** Figure 5 shows the \( \sigma_1 \) value distribution on the top surface of the scored tablets after applying the bending force. Substantial tensile stress is generated around point \( a \) with a change of tablet shape.

**Fig. 4. Experimental Setup for Measuring Dividing Strength of Scored Tablets**

The scored tablet was fixed on the horizontal trestle such that the scored area faces down. A stainless steel probe with a triangle pole blade (45° blade angle and 8 mm blade length) was driven into the tablet until the tablet began breaking. \( W_A \) and \( W_B \) are the weights of each of the halved tablets. Point \( b \) and point \( c \) move horizontally to the left and the right, respectively, after increasing the blade force. Substantial tensile stress is generated around point \( a \) with a change of tablet shape.

**Fig. 5. The Maximum Principal Stress Distribution on the Top Surface of Scored Tablets after Applying the Bending Force**

\( h \): score depth; \( \theta \): score angle.
Fig. 6. The Maximum Principal Stress Distribution on the Lateral Surface of Scored Tablets after Applying the Bending Force
$h$: score depth; $\theta$: score angle; (A): enlarged view of the scored region at $h=1.50\,\text{mm}$.

Fig. 7. The Maximum Principal Stress Distribution on the Top Surface of Scored Tablets after Applying the Diametrical Direction Force
$h$: score depth; $\theta$: score angle.

Fig. 8. The Maximum Principal Stress Distribution on the Lateral Surface of Scored Tablets after Applying Diametrical Direction Force
$h$: score depth; $\theta$: score angle. Maps show the lateral sides faced to the moving rigid wall.
to be a fillet surface to avoid generating a singular point, the edge of V-shape notches often causes the stress concentration. Nevertheless, FEM simulation can be effectively utilized to predict experimental data on the basis of regression analysis (as we discuss later in Fig. 9). The effect of score angles on the $\sigma_1$ value was minimal. Very weak tension was generated on the other site of the top surface apart from the score line when the score was shallow (0.50–0.75 mm).

Figure 6 shows the $\sigma_1$ value distribution on the lateral surface. A tendency similar to that on the top surface was observed on the lateral surface. Strong tensile stress was generated immediately beneath the end of the score and became clear when the score was sufficiently deep (ca. 1.50 mm). Weak tensile force was observed around the end of the scores and the tensile area spread depending on score depth. These results indicate that score depth is more important than score angle for the ease of subdivision and halving equality of scored tablets.

**Effect of Diametrical Compression** Figure 7 shows the $\sigma_1$ value distribution on the top surface of scored tablets after the application of diametrical compression. Weak compression stress was observed in the limited area on the contact surface of the tablet to the rigid wall. A wide range of tensile stresses was generated on the surface in the direction of the diametrical compression axis. The area became wider as a function of score depth, but the effect of score angle was minimal. It is likely that the dominant component on the wide range of the $\sigma_1$ values is tensile strength, which works from the center to the orthogonal direction to the compression axis. Figure 8 shows the $\sigma_1$ value distribution on the lateral surface faces to the rigid moving wall. Interestingly, strong tensile stress was distributed on the center bottom as a bimodal shape, and the area was enhanced with increasing score depth. This suggests that the upper center region is compressed more easily which may lead to the generation of tensile stress on the bottom of the tablet. The sphenoidal shapes of the compressed area may reflect the bimodal shapes of tensile stress generated on the bottom area. This suggests that the tablet became more breakable with increasing score depth.

**Experimental Verification** As a preliminary study, an apparatus mimicking the method shown in Fig. 2 was prepared and used to measure the dividing strength of scored tablet. However, the reproducibility of the experimental result was quite poor. This is because the shape of the tablet is appreciably distorted right before the onset of breakage during the increased bending stress, and the apparatus fails to work on the tablet shape. On the other hand, a reasonable reproducibility of the dividing strength was observed by using the apparatus shown in Fig. 4. It is likely that strong tensile strength generates around the score tip with increasing blade force, and the method substantially reflects the results obtained with FEM simulation. Experimental values such as the dividing strength, halving equality (defined as $F_d$ values), and breaking strength (hardness) are summarized in Table 2. These values were strongly dependent on the score depth and decreased with increasing depth of the score shape. In contrast, the score angle had only a minimal effect on the mechanical values. When the score shape was shallow (0.50–0.75 mm), the $F_d$ value was extremely large and was no longer effective as a dividing line. In general, less than 1% of the $F_d$ value is acceptable for the clinical use of subdividing tablets, in which the therapeutic dose of a drug must be strictly controlled.2,21) A rather deep score (ca. 1.50 mm) was required to ensure good halving equality. However, this may lead to mechanically weak tablets, as summarized in Table 2. The dividing ease and halving equality are features opposed to the mechanical strength of the tablet. The two-way ANOVA results for the dividing strength, halving equality, and hardness are summarized in Tables 3–5, respectively. Both dividing strength and halving equality were significantly affected by the score depth ($h$) and angle ($\theta$) as well as by their interaction, although the effect of score depth on these mechanical characteristics was predominant, as observed in the $F_d$ values (Tables 3, 4). The hardness was significantly affected by the score depth only (Table 5).

### Table 2. Dividing Strength, Halving Equality, and Hardness of Scored Tablets

| Depth, $h$ (mm) | Angle, $\theta$ (°) | Dividing strength ($F_d$ value, %) | Hardness ($F_h$ value, %) |
|-----------------|---------------------|-----------------------------------|--------------------------|
| 0.50            | 45                  | 79.05 ± 1.13                     | 57.94 ± 0.67             |
| 0.75            | 45                  | 71.21 ± 1.13                     | 53.83 ± 0.66             |
| 1.00            | 45                  | 63.37 ± 2.04                     | 3.04 ± 0.86              |
| 1.50            | 45                  | 32.99 ± 1.50                     | 0.66 ± 0.04              |
| 0.50            | 60                  | 70.23 ± 2.04                     | 55.85 ± 0.33             |
| 0.75            | 60                  | 65.66 ± 0.98                     | 9.69 ± 0.34              |
| 1.00            | 60                  | 61.09 ± 1.50                     | 2.64 ± 0.17              |
| 1.50            | 60                  | 26.79 ± 2.26                     | 0.35 ± 0.33              |
| 0.50            | 75                  | 60.76 ± 1.96                     | 53.27 ± 0.69             |
| 0.75            | 75                  | 55.53 ± 1.13                     | 7.68 ± 1.55              |
| 1.00            | 75                  | 51.29 ± 1.50                     | 3.67 ± 0.80              |
| 1.50            | 75                  | 22.87 ± 1.13                     | 0.83 ± 0.33              |

Each datum represents the mean ± S.D. for three determinations.

### Table 3. Two-Way ANOVA for Dividing Strength of Scored Tablets

| Factor              | Degrees of freedom | MS$^{a}$ | $F_{hp}^{b}$ | $p$<sup>c</sup> |
|---------------------|--------------------|----------|--------------|-----------------|
| Depth, $h$          | 3                  | 3225.90  | 1286.39      | <0.0001         |
| Angle, $\theta$     | 2                  | 598.76   | 238.77       | <0.0001         |
| $h \times \theta$   | 6                  | 14.62    | 5.83         | 0.007           |
| Error               | 24                 | 2.51     |              |                 |

$^{a}$Mean square. $^{b}$Observed $F$ value. $^{c}$Risk rate.
Figure 9 shows the relationship of experimental values of dividing strength, halving equality, and hardness to the maximum principal stress around the score line after applying bending force or diametrical direction force. Increasing the $\sigma_1$ value resulted in the improvement of dividing ease and halving equality. But the tablet hardness weakened with increasing the $\sigma_1$ value. Since the FEM simulation results were well-correlated to the experimental results, this technique can be applied to evaluate the score shape of tablets in silico without the need for costly experiments.

**Conclusion**

FEM simulation was used to investigate the mechanical stress on the top and lateral surfaces of scored tablets after application of external forces. When a bending force was applied, strong tensile stress was generated along the score line, which increased with increasing score depth. A wide range of tensile stresses was generated on the top and lateral surfaces of scored tablets after applying diametrical compression. The area became wider as a function of score depth. A reasonable relationship between FEM simulation and experimental results was observed, suggesting that FEM simulation is advantageous for designing scored tablets. Further investigation will be needed for the quantitative prediction of pharmaceutical characteristics of scored tablets. Nevertheless, FEM simulation is useful for improving the understanding of the pharmaceutical characteristics of scored tablets.

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**Conflict of Interest** The authors declare no conflict of interest.

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