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Selection of a round convex tablet shape that mitigates the risk of chipping and capping based on systematic evaluation by utilizing multivariate analysis

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ABSTRACT

Selecting a tablet shape that minimizes the risk of chipping and capping during manufacture is important in pharmaceutical industry. Here, the selection was performed based on systematic evaluation for the first time. Abrasion and stress relaxation time were utilized as indices of the occurrences of chipping and capping, respectively. Partial least square regression models that used tablet shape parameters to estimate the tablet's abrasion and stress relaxation time were utilized to develop response surface plots of the effect of the tablet shapes on the occurrence of chipping and capping systematically, and to identify an optimum tablet shape that is expected to have a low occurrence of chipping and capping. A verification study using commercial scale facilities proved that the optimum tablet shape had a lower occurrence of chipping and capping compared to suboptimum examples as speculated by their abrasion and stress relaxation time. The observed mathematical relationship between the tablet shapes and the occurrence of chipping and capping were consistent with the previous studies based on the comparison of limited number of tablet shapes using different formulations. Consequently, it is expected to be applicable to other formulations beyond the evaluated formulation in the present study.

1. Introduction

Tablets are a common pharmaceutical solid dosage form consisting of one or more active ingredients in combination with excipients. In general, tablets are manufactured by compression of a powder blend or granules, and a polymer coating is often applied to the tablets. The tablets are packed in blisters or bottles to be shipped to hospitals or community pharmacies. Physical defects of the tablets are one of the most common problems resulting from the compression process and the following processes of handling, coating, packaging, and shipping, since the physical defects will have a negative impact on critical quality attributes such as assay, content uniformity, and visual appearance.

Fig. 1 shows two common types of tablet physical defects. The physical defect provided in Fig. 1 (a), generally called chipping, is the loss of a small portion at the edges or the cup surface. Chipping is considered to be due to a low inter-granular binding force that apart from chipping also leads to low tablet hardness and high friability. Fig. 1 (b) shows a partial or complete separation of the cup portion of the tablet, generally called capping. It was considered that the elastic recovery of a tablet after compression is one of the primary causes of the physical defects including capping, which is correlated with other reported root causes such as die-wall pressure during decompression, non-uniform density and stress distribution in a tablet. Air entrapment at the compression has also been known as one of the other common root causes of capping, which can be solved by prolonging the total compression time (Tanino et al., 1995). Garr and Rubinstein (1991) reported that the occurrence of capping increased as the elastic energy stored at the end of compression, i.e., the residual die-wall pressure, which causes elastic recovery during decompression, became high. The non-uniformity of shear stress and density distributions in a tablet are caused by the elastic recovery, which was considered to be the root cause of chipping and capping during the tableting process and the following processes (Wu et al., 2008; Akseli et al., 2013). The type of the physical defects derived from the tablets' elastic recovery depends on the tablet shape (Wu et al., 2008). Akseli et al. (2013) reported that the elastic properties of a tablet measured after the compression also correlated with the capping tendency, whereas Garr and Rubinstein (1991) and Wu et al. (2008) focused on the stress relaxation and elastic

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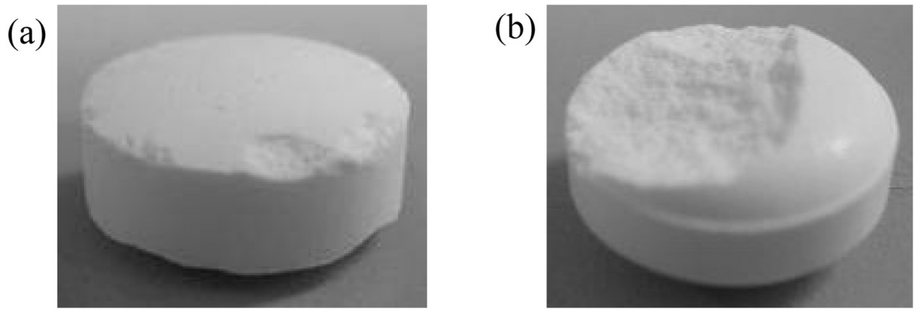

Fig. 1. Typical cracks in 8 mm diameter tablets. (a) Chipping. (b) Capping.

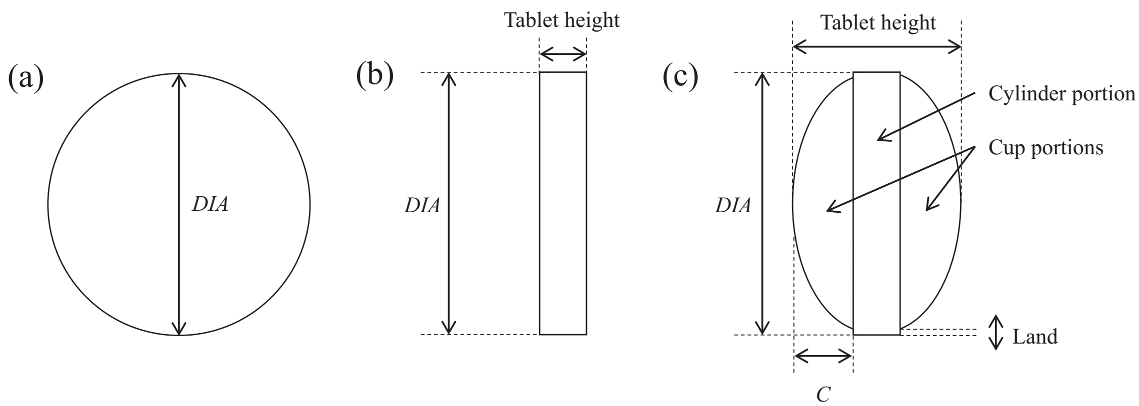

Fig. 2. Round tablet shapes. (a) Top view. (b) Side view of a flat-faced cylindrical tablet. (c) Side view of a convex tablet.

recovery during the compression process.

Tablet shape is one of a number of factors affecting the mechanical strength of tablets, even among round tablet shapes. The round tablet is recognized as the most common tablet shape, usually consisting of a cylinder portion with a flat face or convex as shown in Fig. 2. In most cases the curvature of the convex cup portion is composed of a single or double radius. Fig. 3 shows the definitions of the parameters that constitute a single or double radius cup portion. *R1*, *R2*, cup depth (*C*), diameter (*DIA*), land, α, and β define the cup portion. The value obtained by dividing *C* by *DIA* can be used to classify a convex tablet into categories such as a shallow convex (*C/DIA* = ca. 0.07), standard convex (*C/DIA* = ca. 0.10), deep convex (*C/DIA* = ca. 0.13), and extra deep convex (*C/DIA* = ca. 0.19). Chowhan et al. (1992) reported that the friability of extra deep convex tablets was lower than that of standard and deep convex tablets. Wu et al. (2008) reported that single radius standard convex tablets had a higher occurrence of capping compared to single radius shallow convex and flat-faced cylindrical tablets, whereas the single radius shallow convex and flat-faced cylindrical tablets had a higher occurrence of chipping. The type of the physical defects correlated with the tilt angle of intensive shear stress band at the edge of cup portion during decompression estimated by X-ray tomography and finite element (FE) modeling in the same study. The tilt angle of the intensive shear stress band against compression direction was larger in the single radius standard convex tablet compared with the single radius shallow convex tablet and flat-faced cylindrical tablets. The larger tilt angle of the intensive shear stress band was considered to facilitate the separation of the cup portion in the single radius standard convex tablet. On the other hand, the low tilt angle of the intensive shear stress band against compression direction lead to the loss of a small portion at the edge of the cup portion in the single radius shallow convex tablet and flat-faced cylindrical tablets (Wu et al., 2008). Laity et al. (2010) reported that flat-faced cylindrical tablets had a higher occurrence of chipping compared to that of the single radius extra deep convex tablets. The results by small-angle X-ray scattering (SAXS) measurement and FE modeling showed that the flat-faced cylindrical tablets had a low density part at the bottom corners

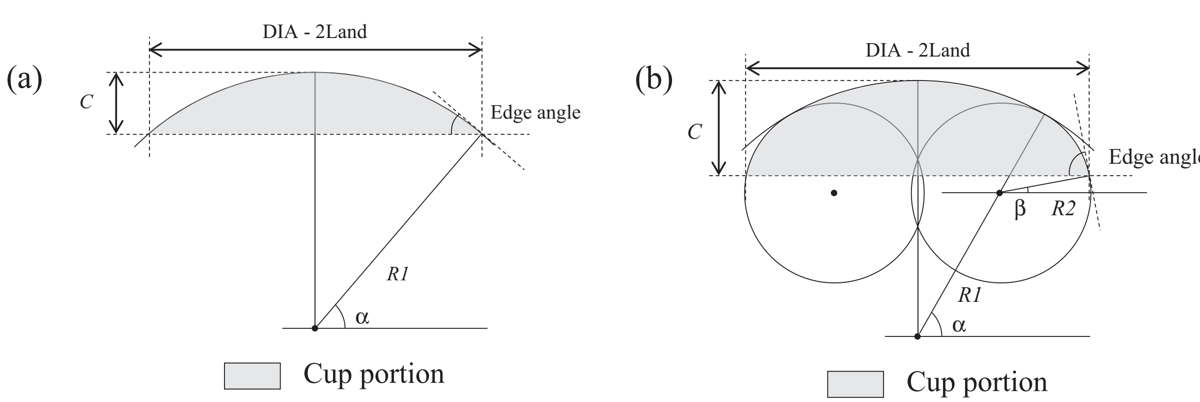

Fig. 3. Definitions of the parameters that constitute a single or double radius cup portion. (a) Single radius convex cup portion. (b) Double radius convex cup portion.