Influence of Rate of Force Application During Compression on Tablet Capping

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ABSTRACT: Root cause and possible processing remediation of tablet capping were investigated using a specially designed tablet press with an air compensator installed above the precompression roll to limit compression force and allow extended dwell time in the precompression event. Using acetaminophen–starch (77.9:22.1) as a model formulation, tablets were prepared by various combinations of precompression and main compression forces, set precompression thickness, and turret speed. The rate of force application (RFA) was the main factor contributing to the tablet mechanical strength and capping. When target force above the force required for strong interparticulate bond formation, the resultant high RFA contributed to more pronounced air entrapment, uneven force distribution, and consequently, stratified densification in compact together with high viscoelastic recovery. These factors collectively had contributed to the tablet capping. As extended dwell time assisted particle rearrangement and air escape, a denser and more homogenous packing in the die could be achieved. This occurred during the extended dwell time when a low precompression force was applied, followed by application of main compression force for strong interparticulate bond formation that was the most beneficial option to solve capping problem. © 2015 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 104:1319–1327, 2015

Keywords: mechanical properties; compression; granulation; tableting; formulation; capping; rate of force application; precompression; dwell-time; air compensator

INTRODUCTION

Capping is a term used to describe the partial or complete detachment of a cross-sectional segment from the top or bottom face of a tablet dosage form, occurring immediately after tablet ejection, sometimes during subsequent tablet testing, processing, or handling. The capping problem, when seen, may be mitigated by formulation changes or modification of processing variables. The possible practical remedies on capping issues in respect to formulation perspective are using more plastically deformable materials and increasing amount of binder in the formulation.[1] However, for a registered product, formulation change is not the preferred alternative to resolve the capping problem. Moreover, particularly for a high-dose product, there is limited flexibility to adjust by changes in the formulation.

In the process perspective, identified causative factors in the formulation of tablets may be attenuated by modification of the tablet press operational attributes. Tablet capping has been associated to a number of causes, air entrapment,[2] mechanism of volume reduction during compression,[3] compression speed,[4] viscoelastic recovery (VER),[1,5,6] stress and density distribution,[7] as well as internal shear stress because of die wall pressure.[8] Several approaches have been tried to prevent capping by lowering compression force, reducing compression speed, or decreasing ejection path in die.[4] Often, when capping issues are seen during tableting, their resolution often involves the application of some of the above-mentioned processing approaches and carried out on a trial-and-error basis. Thus, the understanding of the root causes of tablet capping is still deficient. Therefore, there is an impending need to identify the root causes of tablet capping with in-depth understanding in process perspective to provide systematic and effective approaches to resolve capping problems.

This study was initiated to identify the root causes and possible processing strategies to resolve the problem of tablet capping by utilizing a specially designed rotary tablet press with precompression and main compression events. Acetaminophen–starch (77.9:22.1) was used as model formulation. The set precompression thickness (SPT) and main compression thickness could be set by adjusting the position of respective bottom roll. The SPT was the distance between the top and bottom punches at the precompression position without powder in the die. The precompression event was operated based on application of equal force, whereas the main compression event was operated based on equal tablet thickness (Fig. 1). An air cylinder, called the air compensator, mounted over the precompression roll was employed to regulate the applied force to a maximum preset value by regulating the air pressure. At the precompression event, if the precompression force exceeded the preset limiting force, the air compensator on which the precompression roll was mounted would withdraw the roll upwards, referred as displacement, and thereby maintaining a relatively constant applied force on the compact, whereas the dwell time (time at maximum force)[9] would be extended accordingly. The actual thickness of the compact at precompression was the summation of SPT and displacement. With decreasing SPT, the precompression force should reach in a faster rate to the preset limiting force providing higher displacement and longer dwell time (Fig. 2). Thus, with constant die fill, the dwell time at the precompression could be extended by lowering the turret speed, the precompression force, and/or

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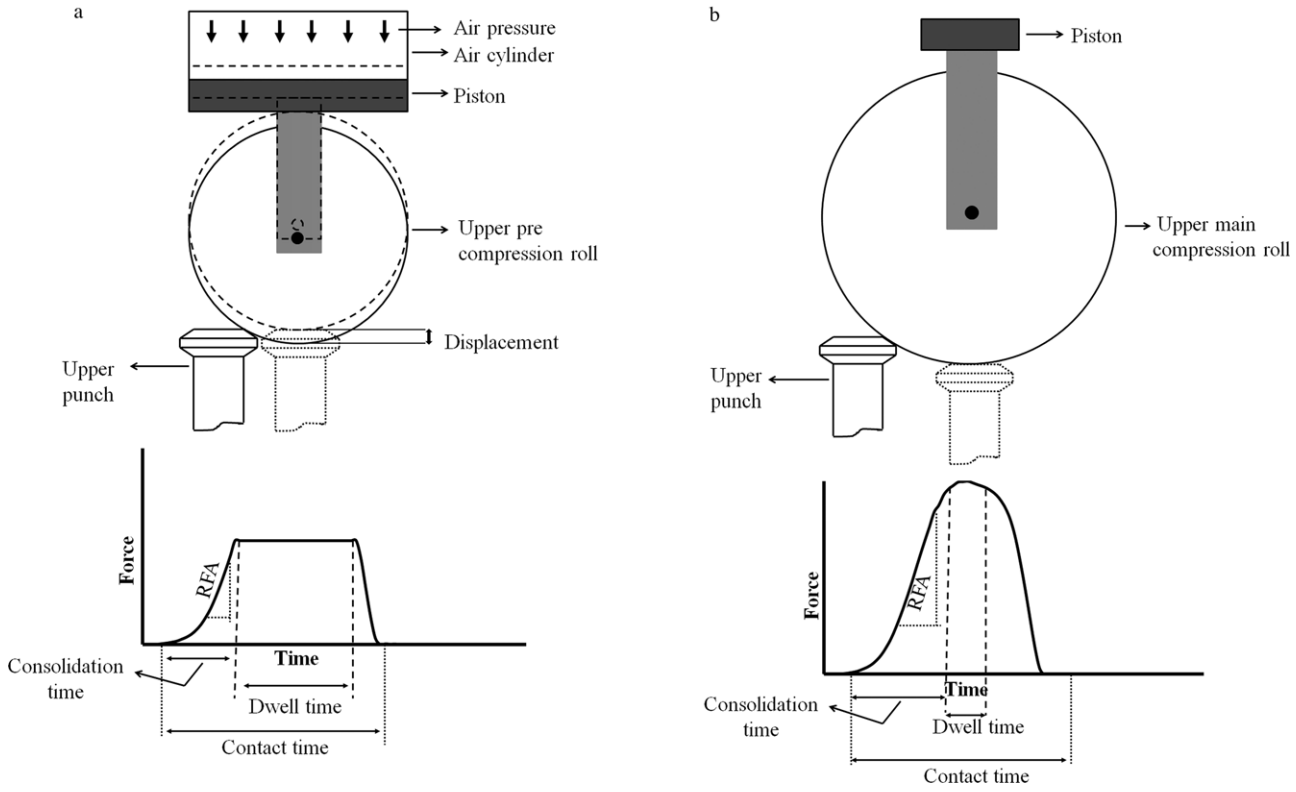

Figure 1. Schematics depicting the graphical representation of compression profile, dwell time, and RFA in (a) precompression event where top precompression roll mounted on an air compensator and (b) main compression event.

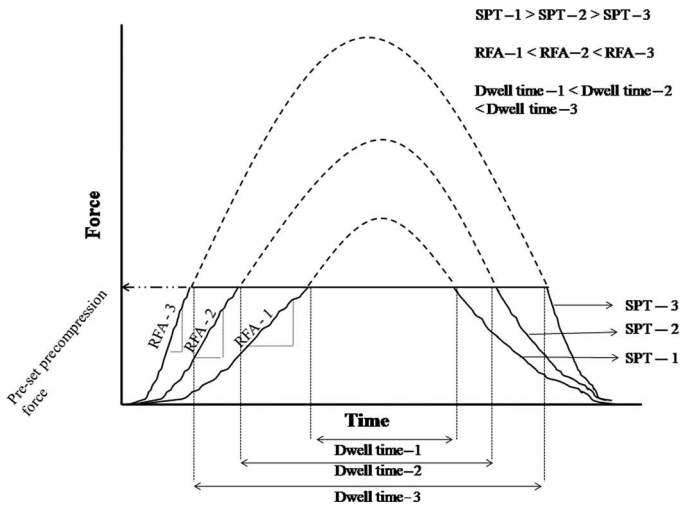

Figure 2. Schematics depicting the graphical representation of precompression compression profile, RFA, and dwell time with different SPT (set precompression thickness)---projected force profile without air compensator.

the SPT. In case of overfill and underfill die, the displacement as well as dwell time increased and decreased, respectively, but precompression force remained relatively constant at the preset value. At the main compression event, the tablet feed compressed to the thickness set for the event. The compression force was higher and lower in case of overfill and underfill die, respectively. Therefore, the dwell time at main compression event could only be extended by reducing the turret speed.

EXPERIMENTAL

Materials

Acetaminophen (Rhodadap Dense Powder; Rhodia Wuxi Pharmaceutical, Jiangsu, China), potato starch (Roquette, Lestram, France), colloidal silicon dioxide (Aerosil 200; Evonik Degussa GmbH, Frankfurt, Germany), and magnesium stearate (M125; Productos Metalest, Zaragoza, Spain) were used in the tablet formulation.

Granule Preparation

Granules containing acetaminophen (77.9%, w/w) and potato starch (22.1%, w/w) were prepared by high shear processor (UltimaPro 10L; GEA-Collette, Wommelgem, Belgium). A portion of potato starch (2.2%, w/w) was used to prepare starch paste in water (15.2%, w/w, solids) that served as binder. Acetaminophen and remaining portion of potato starch (19.9%, w/w) were added to the mixing bowl of high shear processor and dry mixed for 2 min at impeller speed of 450 rpm. The starch paste was then rapidly poured in with continued massing for 5 min using the impeller and chopper operating at speeds of 450 and 2800 rpm, respectively. Granules produced were delumped by passing through a cone mill (Comil197S; Quadro Engineering, Waterloo, ON, Canada) at an impeller speed of 1239 rpm using a square-hole screen of aperture size 6350 μm. The screened granules were then dried in a fluidized bed drier (STREA-1; GEA-Aeromatic, Bubendorf, Switzerland) at 45°C

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