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Interfacial elastic relaxation during the ejection of bi-layered tablets

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ABSTRACT

The predilection of a bi-layered tablet to fail in the interface region after its initial formation in the compaction process reduces its practicality as a choice for controlled release solid drug delivery system. Hence, a fundamental appreciation of the governing mechanism that causes the weakening of the interfacial bonds within the bi-layered tablet is crucial in order to improve the overall bi-layered tablet mechanical integrity. This work has shown that the occurrence of the elastic relaxation in the interface region during the ejection stage of the compaction process decreases with the increase in the bi-layered tablet interface strength. This is believed to be due to the increase in the plastic bonding in the interface region. The tablet diametrical elastic relaxation affects the tablet height elastic relaxation, where the impediment of the tablet height expansion is observed when the interface region experiences a diametrical expansion.

1. Introduction

A multi-layered tablet is a tablet that has more than one individually compacted powder layers within its final single body. For example, a bi-layered tablet consists of two sequentially compacted layers that form a single final coherent tablet body at the end of the compaction process. Multi-layered tablets are favoured due to their controlled release profiles of the active ingredients dissolution profiles (Wu and Seville, 2009). However, the relatively low strength of the interfacial bonding between the adjacent layers (Inman, 2008) signifies the tendencies of the multi-layered tablets to delaminate in the interfacial regions during its manufacture. The maximisation of the interface strength in achieving a mechanically coherent multi-layered tablet requires a considerable trial and error approach as adopted by the pharmaceutical industry. Thus a fundamental understanding of the governing mechanism of the interfacial failure will aid the production of the multi-layered tablets.

In the case of the bi-layered tablets, it has recently been suggested that the relative in-homogeneous profiles of the interfacial fracture and the diametrical surfaces obtained through surface topographical measurements (Inman et al., 2007) are the consequences of the uneven dissipation of the stored elastic energy within the interfacial region during the compaction process (Inman et al., 2009). The in-homogeneous release of the interfacial stored elastic energy in the interfacial region of the bi-layered tablet occurring from the onset of the unloading stage until it is ejected from the die is considered detrimental to its mechanical coherency as a single tablet body (Inman, 2008). Nevertheless, the bi-layered tablet elastic relaxation characteristics derived from the study of the ejected tablet surface and physical dimension might significantly differ from those actually occurring during the compaction process due to the time-dependent elastic relaxation (Silvennoinen et al., 2000; Picker, 2001; Nam et al., 2003). In addition, Train (1956) and Long (1960) suggested that the mechanical integrity of a single compacted tablet most probably be compromised during the ejection stage of the compaction process, due to the elastic relaxation of the tablets in the diametrical and height directions. Hence, it is considered prudent to record the elastic relaxation behaviour of the tablets during the compaction process itself in order to accurately elucidate the influence of the elastic relaxation on the bi-layered tablet mechanical integrity during the ejection stage.

It is the aim of this current work to elucidate the interfacial elastic relaxation behaviour of the bi-layered tablet during the ejection stage and its influence on the final ejected bi-layered tablet mechanical integrity. This is achieved via the accurate online measurements of the tablet dimensions during the ejection stage (Anuar and Briscoe, 2009).

2. Material and methods

2.1. Material

Microcrystalline cellulose (Avicel PH102, FMC U.S.A.) was used as the base material in the formation of the bi-layered tablets. It

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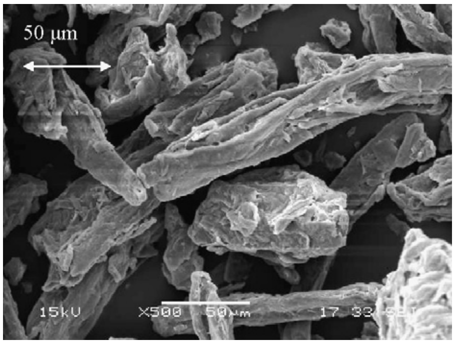

Fig. 1. SEM picture of the Avicel powder (×500 magnification).

was used as supplied by the manufacturer and will be referred to as Avicel in this paper. Fig. 1 shows the SEM picture of the Avicel powder used in this work.

2.2. *Bi-layered tablet formation*

In this work, a universal testing machine with a 50 kN load cell was used in the formation of the Avicel bi-layered tablets (model EZ-50, Lloyds U.K.) in an unlubricated 12.94 mm diameter die set (Specac U.K.). The bi-layered tablets were formed consisting of two 0.5 g powder layers sequentially compacted to form single 1 g bi-layered tablets.

Fig. 2 shows the bi-layered tablet compaction cycle, where its formation involves two separate loading stages. Initially, 0.5 g Avicel powder is inserted into the die and compacted to 22.6 MPa compaction stress to form the bottom first layer of the bi-layered tablet. The upper punch is then removed and another 0.5 g Avicel powder is inserted on top of the already formed initial bottom first layer of the bi-layered tablet. The final top second layer compaction stress is then applied to form a final 1 g bi-layered tablet. In the ejection stage, the lower punch is then removed and the bi-layered tablet is ejected from the die by the downward movement of the upper punch. Three final top second layer compaction stress were used; 22.6 MPa, 45.2 MPa and 90.4 MPa, respectively. The compaction velocity was kept constant at 167 μm s^{-1}, with the same velocity used for both the loading and unloading stages. The compliance of the machine has been taken into consideration by examining the elastic response obtained during the compaction of a blank die.

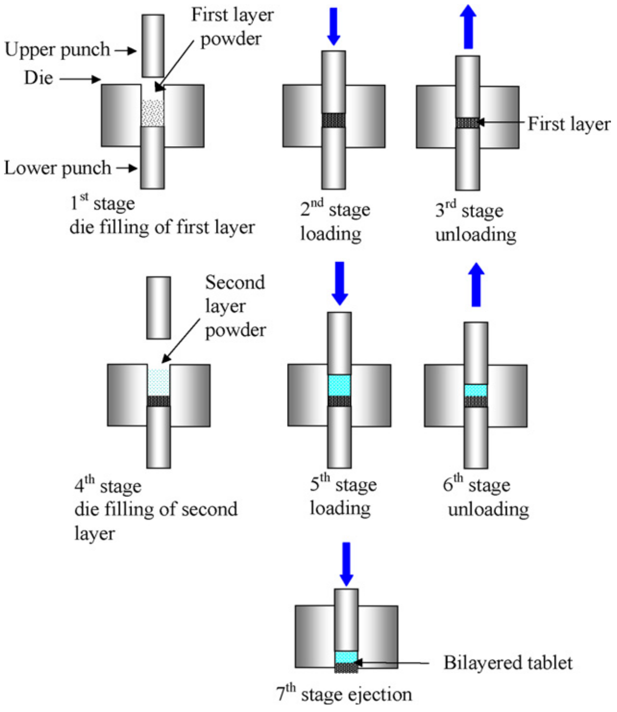

Fig. 2. The bi-layered tablet uniaxial die compaction cycle used in this work.

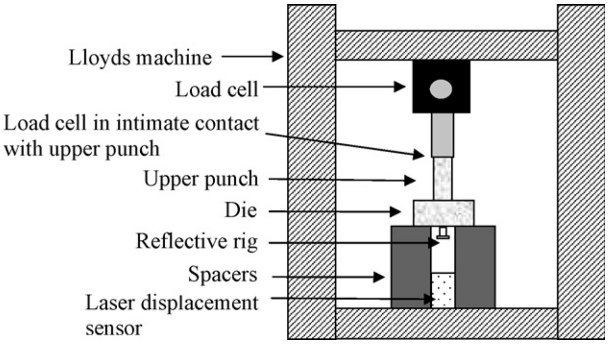

Fig. 3. The ejection rig for the measurement of the tablet height elastic relaxation during the ejection of the tablet from the die cavity. The change in the tablet height is the difference between the recorded load cell displacement and the bottom tablet surface displacement measured by the laser sensor that is fixed at the bottom of the ejection rig.

2.3. *Ejection experiment*

2.3.1. *General preparation procedure*

After the unloading stage, the bottom punch was fully removed before ejecting the bi-layered tablet and the 50 kN load cell was replaced with a 1 kN load cell. Prior to the start of the ejection experiments, the load cell was brought into intimate contact with the upper punch by programming the cross head to move at 16.7 μm s^{-1} until the sensed force is 0.5 N. This position would then be the datum point to mark the start of the ejection experiments.

2.3.2. *Tablet height elastic relaxation study during ejection*

After the removal of the bottom punch, a laser displacement sensor (model LG10A65PIQ, Banner Engineering U.S.A.) is held fixed at the bottom of the ejection rig (Fig. 3). Hence, the laser displacement sensor measures the displacement of the bottom tablet surface as it moves downward during ejection until the tablet is completely extruded from the die cavity with an accuracy of 10 μm.

The relative movement of the tablet counter-faces or the tablet height variation during ejection is then described by:

$$y_b - y_t = \Delta y \tag{1}$$

where y_b is the bottom tablet displacement value measured by the laser sensor and y_t is the corresponding load cell displacement value. y_t is also taken to be the top tablet surface displacement due to the fact that the top tablet surface is adjacent to the moving upper punch, which is in contact with the moving load cell. Therefore, Δy is the change in the tablet height during ejection; a negative value denotes compression and a positive value denotes expansion.

2.3.3. *Tablet diametrical elastic relaxation*

In order to continuously measure the tablet diametrical changes during emergence, a laser micrometer (VG-301, Keyence Corp. Japan) was employed. The laser micrometer was placed 0.5 mm below the die exit (Fig. 4). Therefore, the tablet diameter was measured at the die exit from onset of emergence until complete break away of the tablet from the die cavity with an accuracy of 5 μm.

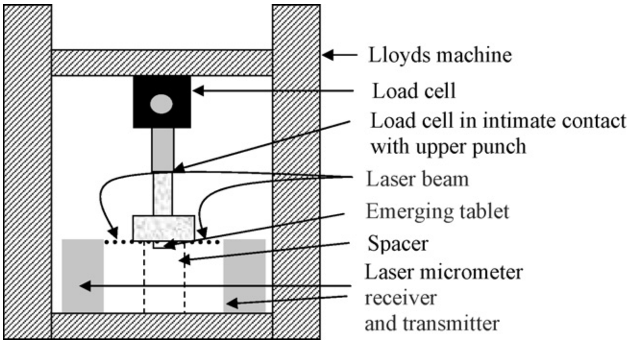

Fig. 4. The ejection rig for the measurement of the tablet diametrical elastic relaxation during the ejection of the tablet from the die cavity.

2.4. Direct tensile strength of the bi-layered tablets

Nyström et al. (1977, 1978) developed a direct axial tensile test in order to measure the tablet axial tensile strength. This is achieved with one of the tablet counter-faces attached to the testing machine and the other fixed, which are then pulled apart (Fig. 5). Inman (2008) further utilised this test in the measurement of the bi-layered tablet axial tensile strength. The tablet would then break in its weakest plane, and in the case of bi-layered tablets, where the interface of the layers is approximately located (Inman, 2008). The tensile force of the tablet is defined as the peak force (P_x) in the force–displacement curve. The tensile strength of the tablet, σ_x can then be estimated by (Nyström et al., 1977, 1978):

$$\sigma_x = \frac{4P_x}{\pi D^2} \qquad (2)$$

where P_x is the measured tablet breaking force and D is the tablet diameter. In this work, two metal platens were glued each onto the tablet top and bottom surfaces using a cyanoacrylate adhesive and were left to dry overnight in order to ensure strong adhesive bonding between them, in accordance to a previous work by Inman (2008). The platens were then connected with one side to the load cell whilst the other side to the fixture on the testing machine through a network of metal chains, as shown in Fig. 5. The load cell was then programmed to move at a velocity of 16.7 μm s^{-1} in the direction that caused the tablet to be pulled apart and undergo a tensile failure. The tensile strength of the tablet is calculated according to Eq. (2).

2.5. Electron microscopy of the bi-layered interfacial fracture surfaces

For the electron microscopy study, the samples were dried overnight in an oven at 103 °C. The non-conductive nature of the tabletted materials required them to be gold coated in a sputter coater. The electron microscope used was JSM 5610 LV (JEOL Ltd. Japan).

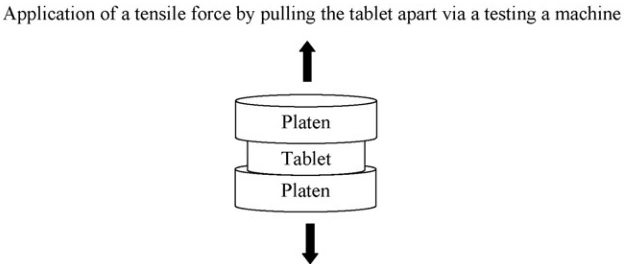

Fig. 5. The direct axial tensile test where the tablet counter-faces are attached to two platens, and placed in tension using a testing machine. The tablet will then fail due to its body being pulled apart.

Table 1
Tensile strengths of the Avicel bi-layered tablets.

Bottom first layer compaction stress/(MPa)	Final top second layer compaction stress/(MPa)	Tensile strength/(kPa)
22.6	22.6	0
22.6	45.2	41.6
22.6	90.4	353.5

3. Results and discussions

3.1. Bi-layered tablet tensile strength

The tensile strengths of the Avicel bi-layered tablets formed in this work have been measured by the use of the direct tensile test method. All the bi-layered tablets failed within the interface region, as viewed physically at the end of the test, in accordance with previous works on the direct tensile strengths of the Avicel bi-layered tablet (Inman, 2008). The overall failure surface is approximately parallel to the tablet counter-faces, albeit some surface irregularities due to the in-homogeneous stress distributions encountered during the formation of the bi-layered tablet (Inman, 2008) that has not been investigated further in this current work.

Table 1 shows the calculated direct tensile strengths of the bi-layered tablets. It can be observed that the tensile strength of the interface region *A* increases with the final top second layer compaction stress. This is believed to be due to the increase in the plastic deformation in the interface causing the increase in the bonding between the two layers and therefore can maintain the residual elastic strains within the region. Figs. 6 and 7 illustrate the SEM images of the fractured bottom layer surfaces at two different top final second layer compaction stresses. As been indicated earlier, the bottom first layer compaction stress is kept constant at 22.6 MPa whilst the top final second layer compaction stress is increased. The increase in the final top second layer compaction stress resulted in a slightly relatively higher deformation of the bottom interfacial fracture surface as observed in the SEM images.

3.2. Bi-layered tablet interface elastic relaxation characteristics

Figs. 8, 10 and 12 illustrate the bi-layered tablet height elastic relaxation profiles whilst Figs. 9, 11 and 13 are the corresponding diametrical elastic relaxation profiles at the different final top second layer compaction stresses. When the first and second layer compaction stresses are equal, an abrupt height expansion-contraction cycle depicted by the sudden increase-decrease in the Δy values in the interfacial region of the bi-layered tablet is clearly observable in Fig. 8. This abrupt tablet height expansion-contraction cycle occurs when the interface (region *A*) emerges from the die cavity. Similarly, a high diametrical elastic fluctuation is depicted in the interface (region *A*) as shown in Fig. 9, giving evidence of the relatively higher stored elastic energy in the region compared to the other sections of the tablet body that displays a relatively smooth profile. The fluctuations in the region *A* are also apparently similar to those observed when the bottom of the bi-layered tablet initially emerges from the die cavity. Therefore, the bi-layered tablet diametrical elastic relaxation profile displays an apparent division at the interface (region *A*), where the overall profile can be divided into two nearly identical separate individual diametrical elastic relaxation profiles, corresponding each to the bottom first layer and the top second layer of the bilayer tablet. This is explicable due to the bottom first layer

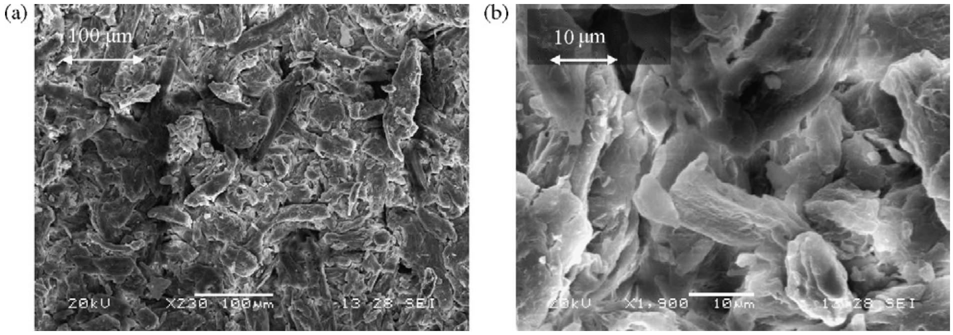

Fig. 6. SEM pictures of the bottom fracture surface of an Avicel bi-layered tablet formed at bottom 1st layer compaction stress = top 2nd layer compaction stress = 22.6 MPa (SEM photo (a) = ×230 magnification, photo (b) = ×1900 magnification).

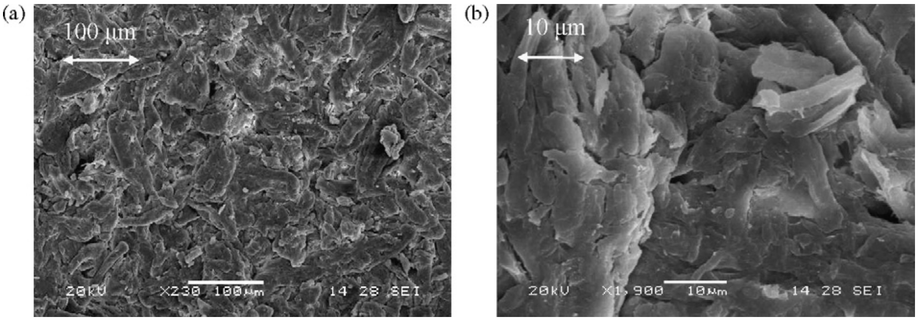

Fig. 7. SEM pictures of the bottom fracture surface of an Avicel bi-layered tablet formed at bottom 1st layer compaction stress = 22.6 MPa, top 2nd layer compaction stress = 22.6 MPa (SEM photo (a) = ×230 magnification, photo (b) = ×1900 magnification).

compaction stress is equal to the final top second layer compaction stress and therefore will most probably exhibit similar diametrical elastic relaxation behaviour. A closer examination of the diametrical elastic relaxation occurring in the region *A* indicates that the tablet diameter appear to 'dip' just before the further diametrical expansion-contractions cycles that follow thereafter. This can be due either to a presence of an interfacial crack on the tablet circumferential surface or the simultaneous slight contraction of the interfacial region *A*. It is then believed that the abrupt height expansion is 'pulling' the tablet axially therefore causing the apparent initial contraction (or crack) in the tablet diameter in the region *A*. The interface will then be severely weakened by the height elastic expansion, which then ultimately lead towards the detachment of the bi-layered tablet into two distinct sections; the bottom first layer and the second top layer, which can be viewed from the diametrical elastic relaxation profile (Fig. 9). According to Inman (2008), the existence of the stored elastic energy in the interfacial region can be ascribed to the in-homogeneous stress distribution during the formation of both the bottom and top layers of the bi-layered tablet. Hence, the release of this stored elastic energy in the interface during the emergence depicted by the sudden increase in the tablet height causes the bi-layered tablet to fail catastrophically across the interfacial region *A* upon ejection.

When the final top second layer compaction stress increases to 45.2 MPa, the abrupt initial height expansion previously observed is absent from the tablet height elastic relaxation profile (Fig. 10). Instead, a tablet height contraction is present in the interface (region *A*), after which the tablet height slowly increases depicted by the more positive Δy values as the tablet emerges further from

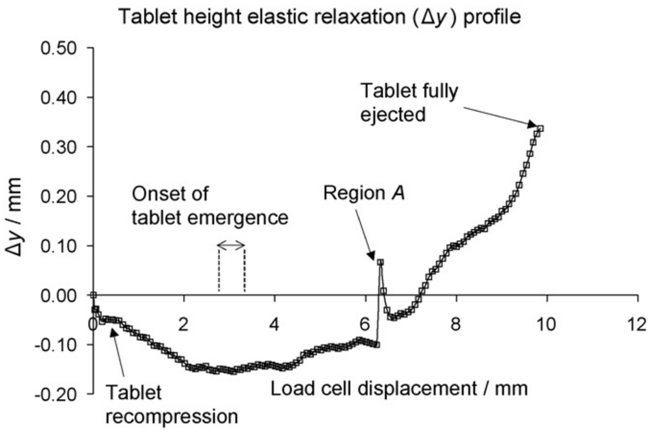

Fig. 8. The Avicel bi-layered tablet height elastic relaxation and the ejection force profiles (bottom first layer compaction stress = final top second layer compaction stress = 22.6 MPa). Note the abrupt elastic expansion in the interface region *A*.

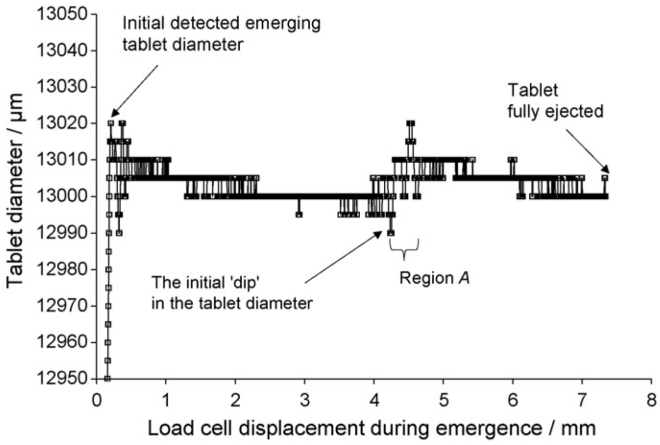

Fig. 9. The Avicel bi-layered tablet diametrical elastic relaxation profile (bottom first layer compaction stress = 22.6 MPa, final top second layer compaction stress = 45.2 MPa). Note that the profile is apparently divided at the interface region *A* into two parts.

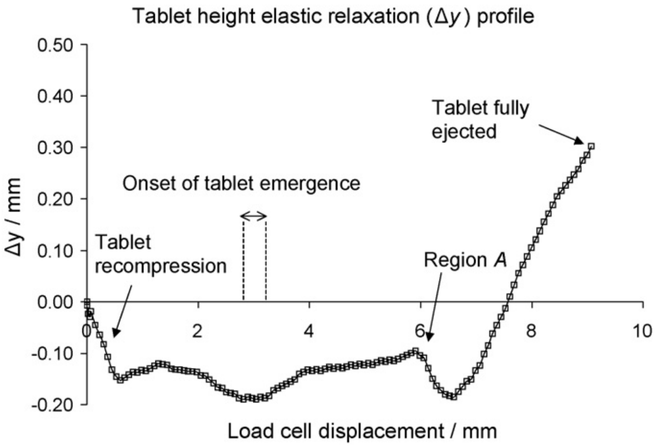

Fig. 10. The Avicel bi-layered tablet height elastic relaxation and the ejection force profiles (bottom first layer compaction stress = 22.6 MPa, final top second layer compaction stress = 45.2 MPa). Note the apparent contraction observed in the tablet height, depicted by the decrease in the Δy values in the interface region *A*.

the die cavity. The corresponding diametrical elastic relaxation profile illustrates that the diametrical expansion in the interface encompasses a larger portion of the final top second layer (region *A*) in comparison to the previous lower compaction stress of 22.6 MPa in Fig. 11. Therefore, it is apparent that the interface (region *A*) experiences simultaneous diametrical expansion and height contraction. The interface expands in the diametrical direction and therefore ‘pulling’ or contracting slightly the tablet height, which is undergoing a continuous elastic expansion (Fig. 10). It is also assumed that the interfacial region *A* has deformed plastically to a greater extent at the final top layer compaction stress of 45.2 MPa compared to the lower final top layer compaction stress of 22.6 MPa. The plastic bonding between the interface (region *A*) will to some extent counteract the height and diametrical elastic relaxations, resulting in the relatively gradual stretching-contraction of the interface region *A* (Figs. 10 and 11), in comparison to the manner seen in the previous case (Figs. 8 and 9). It also seems that that the retardation effect of the localised diametrical elastic relaxation in the interface lowers the final Δy (the final tablet height expansion measured at the end of the ejection stage) as observed in the tablet height elastic relaxation profiles (Figs. 8 and 10). Fig. 12 illustrates that when the final top second layer compaction stress is further increase to 90.4 MPa, the interface region *A* does not suffer any apparent contractions or expansions, only a slight impediment of the tablet height expansion depicted by the nearly constant Δy values before the tablet height expands again as the tablet emerges further from the die cavity. Likewise, the diametrical elastic relaxation profile (Fig. 13) also does not indicate the presence of any apparent diametrical elastic fluctuations in the interface region. This can be attributed to the increase in the plastic deformation (as shown qualitatively in Figs. 6 and 7) in the interface region leading towards an improvement in the bonding between the two adjacent layers of the bi-layered tablet by counteracting the expansion of the interface region due to the residual elastic strains. Also, the increase in the final compaction stress in the formation of the bi-layered tablet can also reduce the overall stored elastic energy within the interface region due to the plastic flow of the interfacial bonds between the two adjacent layers (Figs. 6 and 7).

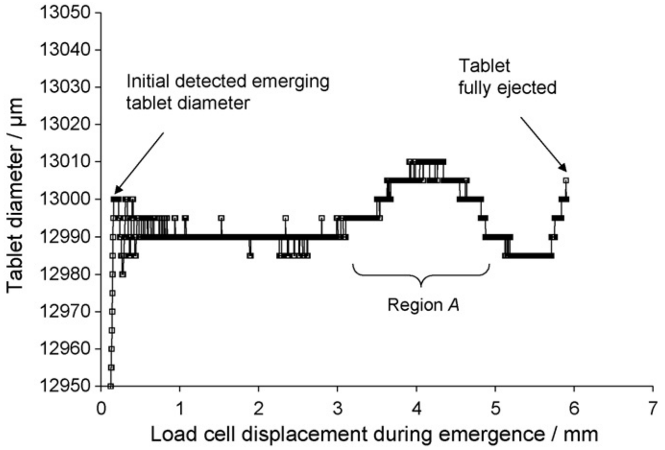

Fig. 11. The Avicel bi-layered tablet diametrical elastic relaxation profile (bottom first layer compaction stress = 22.6 MPa, final top second layer compaction stress = 45.2 MPa). Note the gradual diametrical expansion in the interface region *A*.

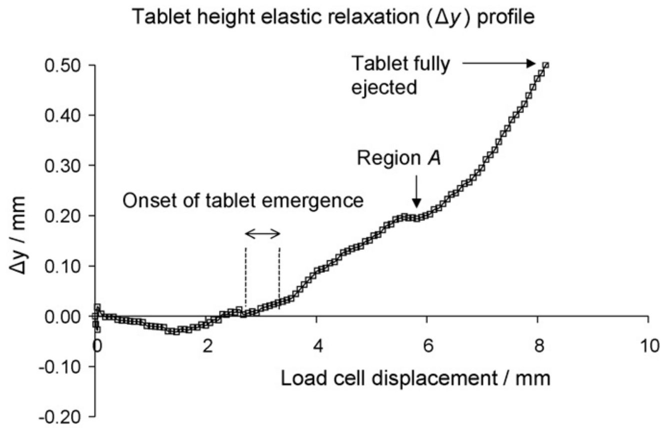

Fig. 12. The Avicel bi-layered tablet height elastic relaxation and the ejection force profiles (bottom first layer compaction stress = 22.6 MPa, final top second layer compaction stress = 90.4 MPa). Note the slight impedement in the tablet height expansion, depicted by the approximately constant Δy values in the interface region *A*.

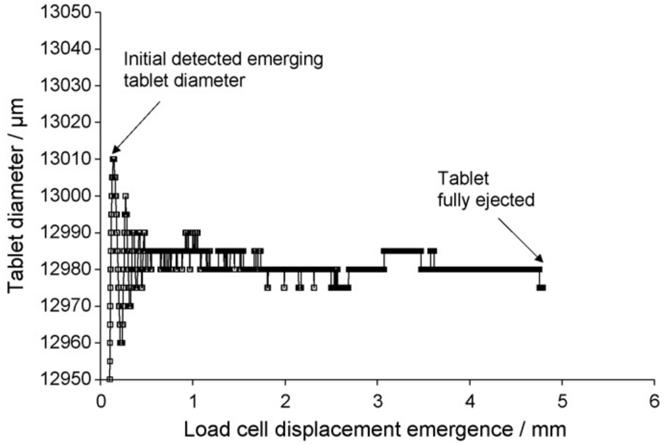

Fig. 13. The Avicel bi-layered tablet diametrical elastic relaxation profile (bottom first layer compaction stress = 22.6 MPa, final top second layer compaction stress = 90.4 MPa).

4. Conclusion

It has been clearly shown that the localised tablet diametrical expansion will to some extent retards its height expansion in the interfacial region. Thus an elastic strain gradient is believed to develop that is detrimental to the bi-layered tablet mechanical integrity in the interfacial region. The influence of the localised elastic relaxation in the interface region decreases when the extent of the plastic deformation increases the bonding between the two layers with the increase in the final compaction stress. This is possibly due to both the decrease in the tablet stored elastic energy, which is the source of the tablet elastic relaxation and the formation of a stronger interfacial bonding between the two adjacent layers that eventually leads to the improvement of the overall bi-layered tablet mechanical integrity.

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