CAFEi2012 - 111

FUNDAMENTALS COMPACTION OF BI-LAYERED TABLETS

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ABSTRACT

Bi-layered tablets are produced by having two pharmaceutical powders, confined within a die, compacted under certain amount of load consecutively one after another. In this study the bi-layered tablets are made of microcrystalline cellulose (MCC), which is commonly used as a binder in pharmaceutical tablets due to its good compaction properties, and lactose which has a poor compactibility in contract to MCC. The objective of this study is to investigate the characteristics and mechanical strength of bi-layered tablets after the ejection process. With variations of processing parameters and raw material compositions the tablets are formed by using the Instron Universal Testing Machine. The compaction load for the bottom layer is kept constant at 3kN (22.6MPa) while the top layer compaction load ranges from 3kN (22.6MPa) to 24kN (180.83MPa). From the compaction process the plastic and elastic energy curves of the powders, the ejection curves as well as the diametrical relaxation of the tablets are observed. Indirect tensile strength test was conducted 24 hours after the ejection process. The plastic and elastic energy for both powders increases with increasing compaction load. The tensile strength of the tablets increases as the compaction loads increases for the top layer. The tablets with microcrystalline cellulose as the top layer have a higher tensile strength in contrast to tablets with lactose as the top layer.

Keywords: *bi-layered tablet, compaction, lactose, microcrystalline cellulose, diametrical relaxation.*

INTRODUCTION

Pharmaceutical or food powders are compressed in a die by the action of two punches; the static lower punch and the moving upper punch which enables the particles to join together through inter-particulate bonding and form solid tablets [1]. With the advancement of technology and high demand for a more convenient way of drugs administration, the bi-layered tablet is introduced to cater different medicinal purposes with its variety range of predetermined release profiles [2]. In contrast to the ordinary single layer tablet, a bi-layered tablet comprises of two pharmaceutical powders which are compacted together consecutively one after another with variation of compaction load for each layer. The compaction load usually differs according to the physical properties of the powders to ensure that optimum condition could be obtained hence less defected bi-layered tablets are produced.

However during the production, packaging and distribution, these bi-layered tablets have the tendency to fracture at the interface of the two adjacent layers. It is also difficult to guarantee that these tablets will stay intact when a certain amount of load is applied onto them. The bi-layered tablets produced must also be weak enough for it to disperse and undergo dissolution once it enters the oral route [3]. In this study, two of the most common pharmaceutical powders which differ in terms of its compatibility are used. Microcrystalline cellulose powder (MCC) is used because it possesses good compaction properties. In contrast to MCC, the lactose powder which has poor compaction properties is also used to provide a variation in the tablet layer arrangements.

The plastic and elastic curves were obtained during the compaction of the tablets in order to understand how each powder behaves when load is applied onto them in a stainless steel die. The ejection curves were also studied to investigate the relationship between the plastic and elastic energy and the maximum ejection stress required to eject the tablets. In addition, the diametrical elastic relaxation is also obtained by using a laser micrometer to detect the diametrical fluctuations of the tablets as it emerges out of the die. This gives a better understanding on how the powder particles behave after the load is removed and also during the ejection of the

tablet. Finally, the strength of the tablets was tested by undergoing the Indirect Tensile Test or commonly known as the Brazilian Test.

MATERIALS AND METHODOLOGY

Raw materials

Microcrystalline cellulose (MCC) powder and lactose powder were used to produce bi-layered tablets in this study. The MCC powder used was Avicel PH 102 and is produced by FMC Biopolymer (U.S.A). Alpha-lactose monohydrate used in this study is produced by Meggle (Germany). The SEM photographs of the powders are shown in Fig. 1 and Fig. 2.

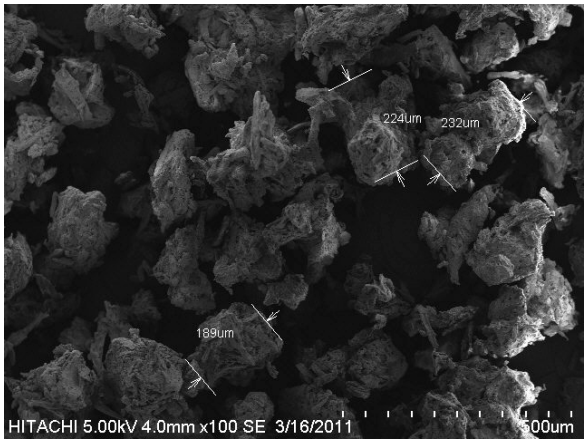

Fig 1: Microcrystalline cellulose powder under X 100 magnification.

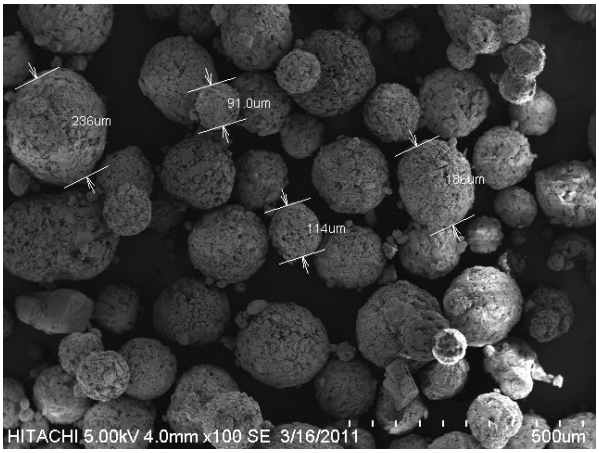

Fig. 2: Lactose powder under X 100 magnification.

e-ISBN 978-967-960-322-4

Tablet compaction and processing parameters

For the production of bi-layered tablets, lactose and MCC are weighed with a 50-50 mass fraction. Both powders are of 0.5 g in weight and thus results in approximately 1.0 g of bi-layered tablets upon ejection. To form the bottom layer, one of the powders was poured into the 13 mm cylindrical stainless steel die (Specac, U.K.) and was then subjected to 22.6 MPa of compacting stress with a universal testing machine (model 3382, Instron, USA). The top layer of the tablet was then formed by pouring the other powder onto the first layer and further subjected to compacting stresses ranging from 22.6 MPa to 180.86 MPa. The process is then repeated by changing the order of the powder for each layer. For each combination the tablets were done in triplicate. Table 1 shows the variety of tablets produced.

Table 1: Different tablet compacting stress variety

Powder for the bottom layer with compacting stress of 22.6 MPa	Powder for the top layer and its compacting stress			
	22.6 MPa	45.21 MPa	90.43 MPa	180.86 MPa
Microcrystalline cellulose	Lactose	Lactose	Lactose	Lactose
Lactose	Microcrystalline cellulose	Microcrystalline cellulose	Microcrystalline cellulose	Microcrystalline cellulose

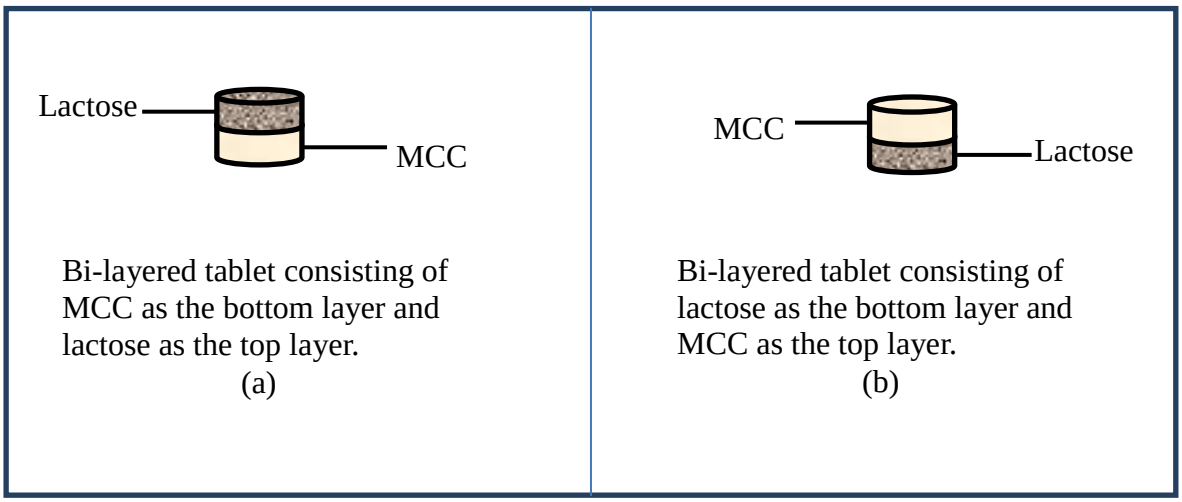

Fig. 3: Bi-layered tablet compositions produced in this study: (a) MCC as bottom layer and lactose as top layer; (b) lactose as bottom layer and MCC as top layer.

The upper punch velocity was set at 0.1 mms^{-1} for the loading process and at 0.0167 mms^{-1} for the unloading process [4]. After compaction of the top layer, the tablet is ejected by removing the bottom punch at a speed of 0.083 mms^{-1}[5]. The tablets produced were stored for 24 hours in a air tight container with silica gel at ambient temperature to allow bonding between the particles before it undergoes the material strength test.

Diametrical elastic relaxation during ejection

During the ejection process where the bottom punch has been removed, a laser micrometer (model VG-301, Keyence, Japan) was placed at the bottom of the die to measure the diameter of the tablet as it moves downwards until the tablet is fully ejected out of the die [6]. The laser micrometer will obtain the diameter reading directly after it sense the emergence of the bottom layer of the tablet. This test was conducted to study the tablet diametrical changes during emergence [6] where it can then be related to the elasticity and plasticity of the powders. The ejection curve was also obtained to identify the maximum stress required to eject the tablet out of the die.

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Diametrical compression test

After 24 hours upon ejection, the tablet undergoes the diametrical compression test or known as the Brazilian test. The tablets were placed between two flatten plates and compressed diametrically by the Instron Universal Testing Machine with the speed of the upper punch set constant at 0.0116 mms^{-1} [4]. Compression was done until the tablet fractures. The maximum load that the tablet withstands before undergoing complete fracture is known as the maximum tensile strength of the tablet. These values were obtained by using the Bluehill software (Canton MA, U.S.A.).

RESULTS AND DISCUSSIONS

Plastic and elastic profiles

The plastic work of both powders increases as the compaction stress is also increased as shown in Fig. 4. When the compression load is varied between 22.6 MPa to 180.86 MPa for the bottom layer it is observed that the plastic work of MCC is higher than that of lactose. This indicates that MCC powders deform predominantly by plastic deformation in contrast to lactose powders.

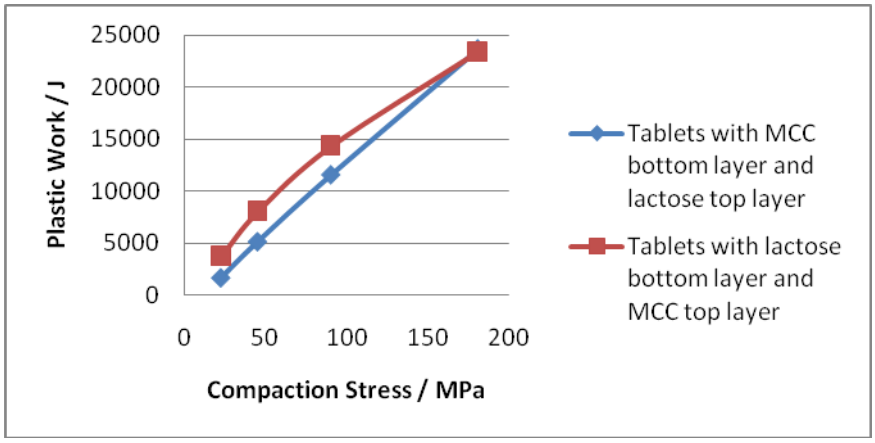

Fig.4: Plastic work at different compaction stresses.

Fig. 5 shows that the elastic work also increases as the compaction stress is increased. The elastic work is however rather similar between the two powders in which is similar to the previous study done by [5].

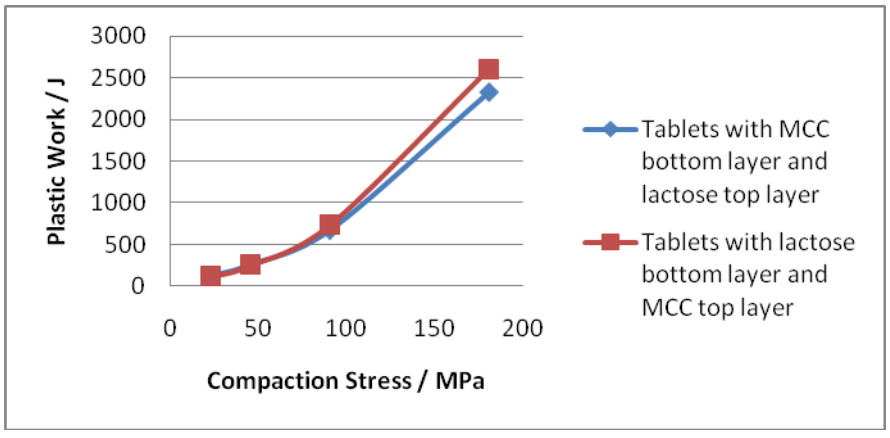

Fig. 5: Elastic work at different compaction stresses.

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Ejection curve

During the ejection of the tablet from the die there is an existence of die wall friction which results in force [6]. This maximum force can be observed by the ejection force curve in Fig. 6. By increasing the compaction stress it is observed that the maximum ejection forces of the tablets are also increased. However, the ejection force of the tablet with lactose as the top layer is higher compared to tablets with MCC as top layer. This means that it is harder to eject for the bi-layered tablets having their top layer made of lactose powders. Hence, this can be attributed to the elastic response of the lactose powders due to the relatively lower plastic work during the loading stage shown in Fig. 4. Also, the increase in the maximum ejection stresses is assumed to exist due to the increase in the stored elastic energy of the tablet with the compaction stress. The tablets, constrained within the die, can only expand axially thus increasing its height during the unloading stage. The tablet also expands radially but it is constrained by the die wall. A higher stored elastic energy indicates that the tablet is pressing harder onto the die walls giving rise to a higher die wall friction thus a higher maximum ejection force in order to push the tablet out from the die.

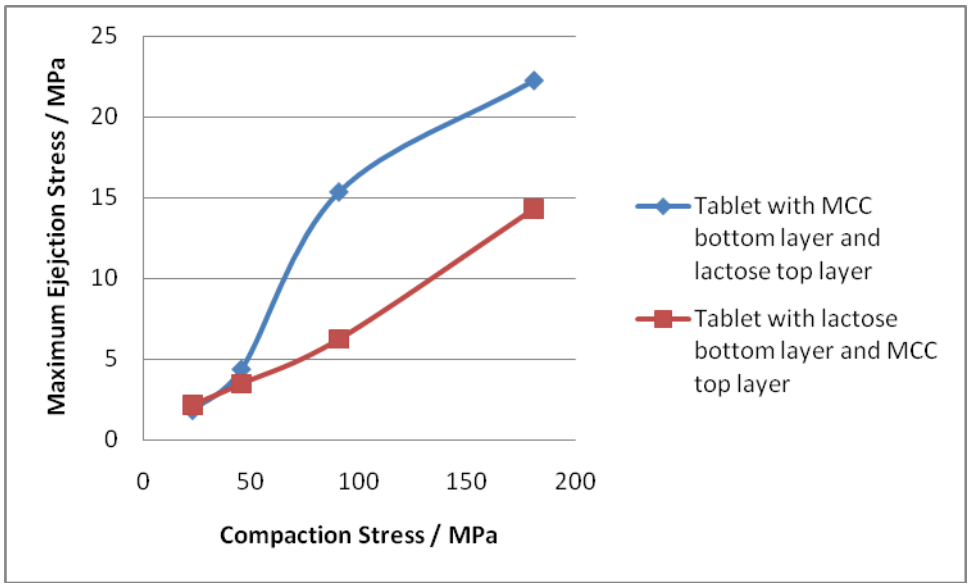

Fig. 6: Maximum ejection stress curve

Diametrical elastic relaxation during ejection

In general, there are variations in the tablet diameter as the tablet emerges from the die cavities which are shown in Fig. 7 to Fig. 14. The diametrical profile becomes highly fluctuated as the top layer compaction stresses increases. It also can be observed that the diametrical fluctuations were more apparent when the top layer is made from MCC. This might indicate the ductility of MCC top layer as it elastically relaxes during emergence from the die cavity.

Meanwhile, lactose exhibit rather smooth profile in comparison to MCC as the top layer. However, it can be observed that in some cases the top half of the bi-layered tablet has a higher diameter in comparison to the bottom half (Fig. 7, Fig. 8, Fig. 9, and Fig. 10). This is mostly absent from the MCC diametrical profiles (Fig. 11, Fig. 12, Fig. 13 and Fig. 14). Therefore, this suggests that the higher die wall radial stresses were acting on the top half of the tablet causing the observed higher energy in the top half. This is most possibly causing the higher maximum ejection stresses that were observed for the lactose top layer tablet (Fig. 6). This is similar to a previous work using paracetamol single layer tablet [7].

In Fig.7 the diametrical profiles of bi-layered tablets made of MCC as the bottom layer (22.6 MPa) and lactose as the top layer (22.6 MPa) are shown. During the first emergence of the bottom layer of the tablets the diameter is directly detected by the laser micrometer resulting in the sudden increase of the diameter reading. The diametrical fluctuations are then relatively constant as the tablets are ejected out of the die. It is assumed that after half of the tablet is ejected, whereby the emergence of the top layer is about to begin, the diameter of

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the tablets relatively increases. This indicates that the stored elastic energy of lactose is causing higher radial expansion of the tablet than that of MCC layer.

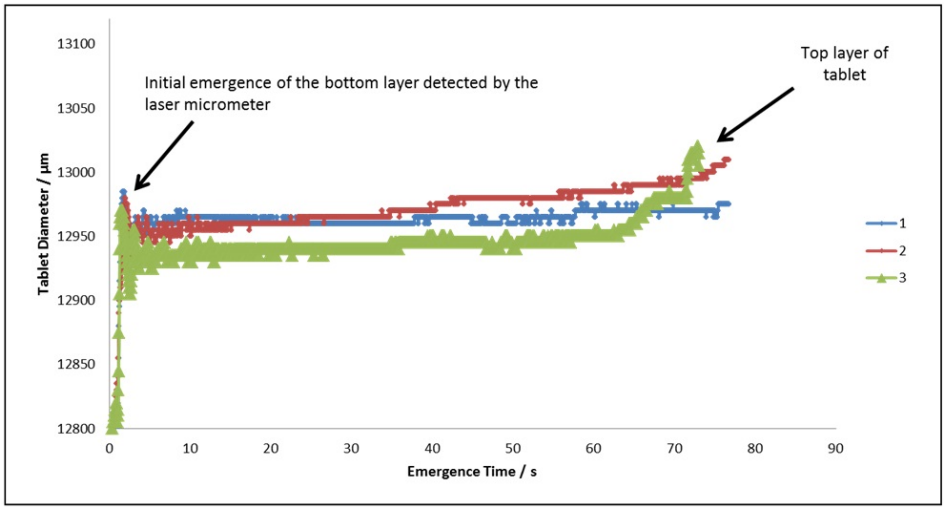

Fig. 7: Tablet diameter versus emergence time during the ejection of bi-layered tablets with MCC as bottom layer (22.6 MPa) and lactose as top layer (22.6 MPa).

In Fig. 8 it shows the diametrical profiles of bi-layered tablets made of MCC as the bottom layer (22.6 MPa) and lactose as the top layer (46.21 MPa). The diametrical fluctuation of these bi-layered tablets suggests the same assumptions as the tablets in Fig. 7.

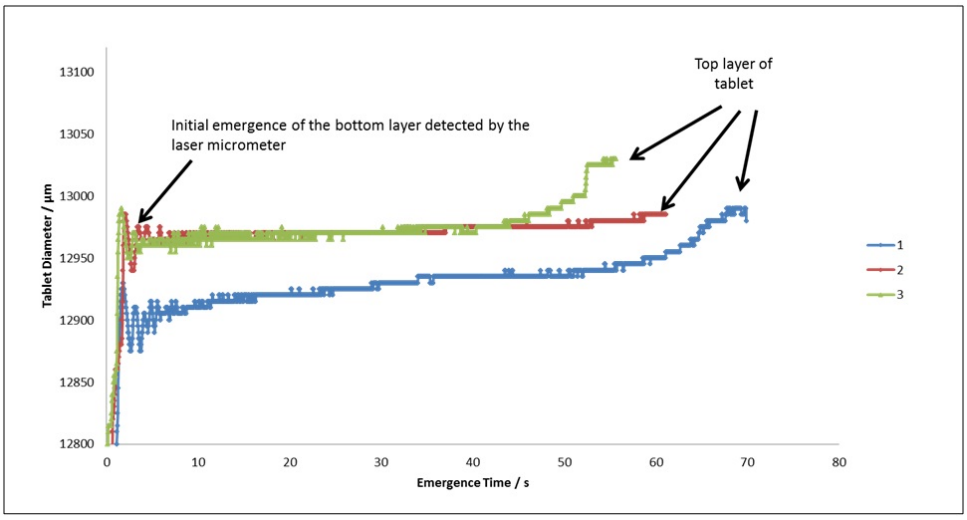

Fig. 8: Tablet diameter versus emergence time during the ejection of bi-layered tablets with MCC as bottom layer (22.6 MPa) and lactose as top layer (46.21 MPa).

In Figure 9 the diametrical profiles of bi-layered tablets made of MCC as the bottom layer (22.6 MPa) and lactose as the top layer (90.43 MPa) are shown. Due to the high compaction stress of the second top layer it can be observed that the sudden diametrical increase during the first emergence of the tablet is relatively higher than tablets of lower compaction stresses for the top second layer. This indicates the strong force that repels the die wall due to the existence of high elastic energy.

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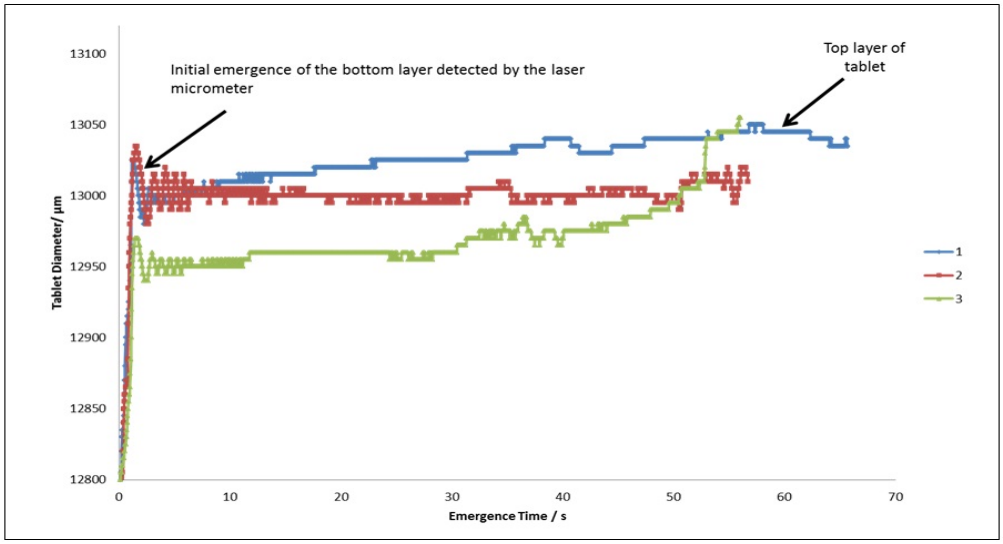

Fig. 9: Tablet diameter versus emergence time during the ejection of bi-layered tablets with MCC as bottom layer (22.6 MPa) and lactose as top layer (90.43 MPa).

In Figure 10 the diametrical profiles of bi-layered tablets made of MCC as the bottom layer (22.6 MPa) and lactose as the top layer (180.86 MPa) are shown. The diametrical profiles of these tablets suggest the same assumptions as tablets in Figure 9.

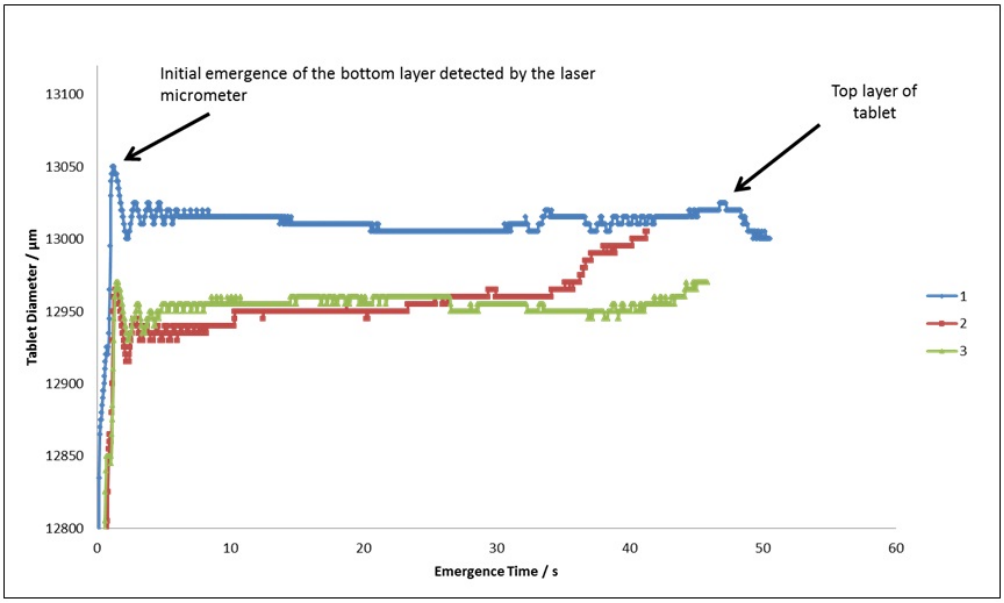

Fig. 10: Tablet diameter versus emergence time during the ejection of bi-layered tablets with MCC as bottom layer (22.6 MPa) and lactose as top layer (180.86 MPa).

Figure 11 shows the diametrical profiles of bi-layered tablets made of lactose as the bottom layer (22.6 MPa) and MCC as the top layer (22.6 MPa). The sudden increase in diameter during the emergence of the first bottom layer indicates the high repulsion of the tablets towards the die wall. The profiles fluctuate indicating the instability of the tablet diameter due to the stored elastic energy in the tablet which causes the tablet to expand radially. This also indicates the ejection stresses depicted in Figure 6.

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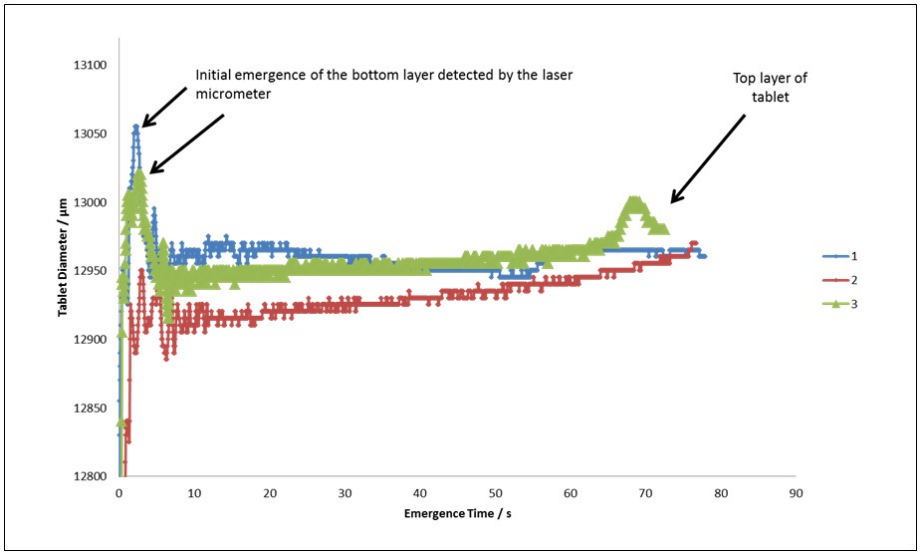

Fig.11: Tablet diameter versus emergence time during the ejection of bi-layered tablets with lactose as bottom layer (22.6 MPa) and MCC as top layer (22.6 MPa).

Figure 12 shows the diametrical profiles of bi-layered tablets made of lactose as the bottom layer (22.6 MPa) and MCC as the top layer (46.21 MPa). The bi-layered tablets for this variations shows the same behaviour in terms of diametrical fluctuations. Similar to the tablets in Figures 7-10 the bi-layered tablets are assumed to be partially ejected when there is an increase in the diameter.

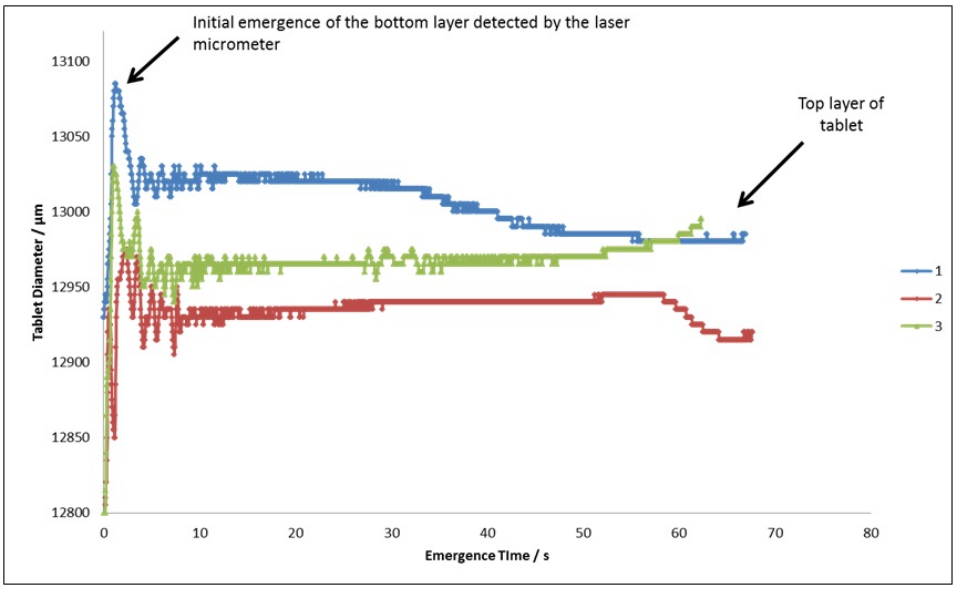

Fig. 12: Tablet diameter versus emergence time during the ejection of bi-layered tablets with lactose as bottom layer (22.6 MPa) and MCC as top layer (46.21 MPa).

In Fig. 13 the diametrical profiles of bi-layered tablets made of lactose as the bottom layer (22.6 MPa) and MCC as the top layer (90.43 MPa) are shown. The diametrical increase during the first emergence is relatively higher than tablets with lower compaction stress (22.6 MPa and 46.21 MPa) due to the high stored elastic energy. However, in contrast to the tablets in Fig. 11 the diametrical fluctuations are relatively lower.

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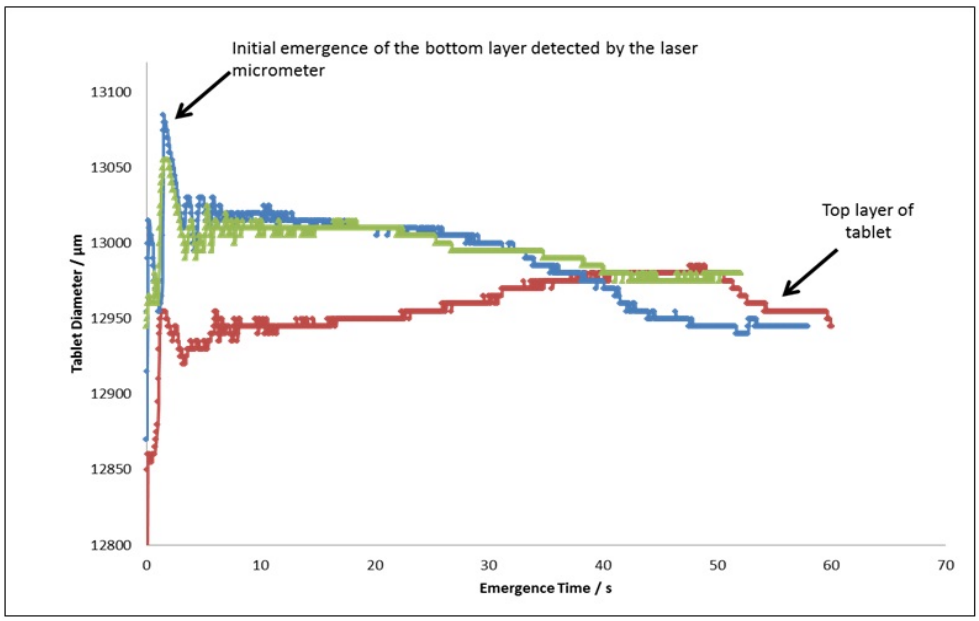

Fig. 13: Tablet diameter versus emergence time during the ejection of bi-layered tablets with lactose as bottom layer (22.6 MPa) and MCC as top layer (90.43 MPa).

Figure 14 shows the diametrical profiles of bi-layered tablets made of lactose as the bottom layer (22.6 MPa) and MCC as the top layer (180.86 MPa). Under high compaction stress the tablets exhibit a very steep increase in the diameter of the first tablet emergence. The fluctuations during the ejection of the tablets are relatively higher assumed to be caused by the much higher repulsion and stored elastic energy compared to the tablets in Figures 11-14.

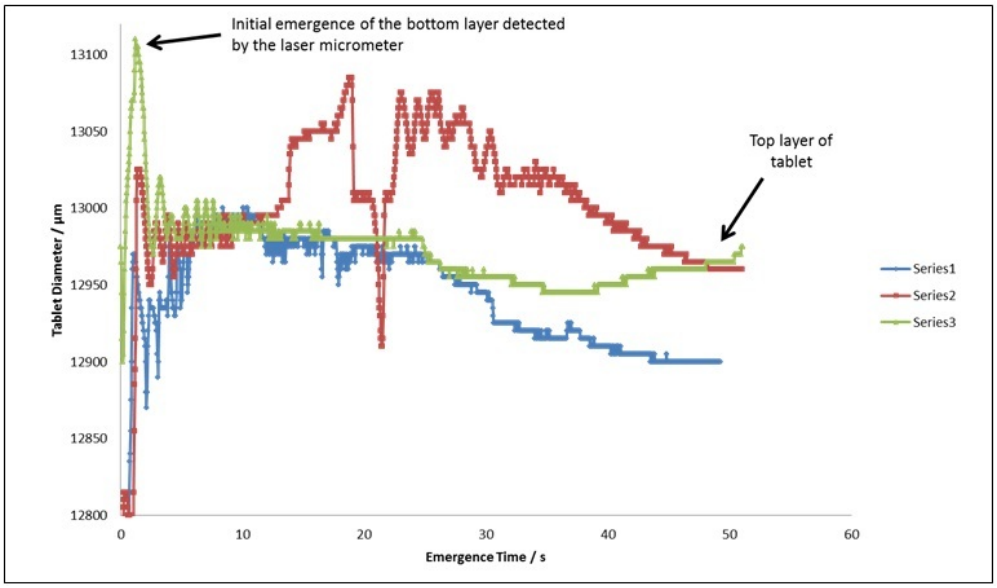

Fig. 14: Tablet diameter versus emergence time during the ejection of bi-layered tablets with lactose as bottom layer (22.6 MPa) and MCC as top layer (180.86 MPa).

Mechanical strength of tablets

The bi-layered tablet strength is compromised when the top layer is made of lactose powders. This can be seen in Fig. 15 where the tensile strength of the tablets is estimated by using the Brazilian Test. This is most probably due to the low plastic energy and high maximum ejection stresses during ejection that compromises the mechanical integrity of the bi-layered tablets made from lactose as the top layer. The increase in the compaction stresses facilitate the interparticulate bonding therefore the tensile strength of the tablets also increases with compaction stress as shown below.

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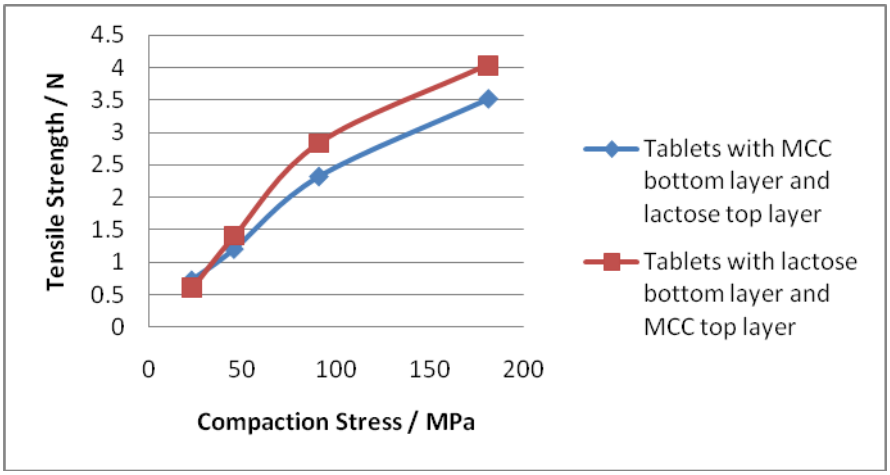

Fig. 15: Tensile strength of bi-layered tablets at different compaction stresses.

During the initial stage of the Brazilian Test, it was found that the layer comprising of lactose will start to fracture first. However, the whole tablet is still in contact and has not failed yet. As the load is continuously applied onto the tablet the MCC layer will start to slowly crack. At this point lactose has totally cracked but the whole tablet strength is held by the elastic MCC layer. After the tablet is considered to have undergone total failure in terms of strength the cracked tablet was observed. This is shown in Fig. 16.

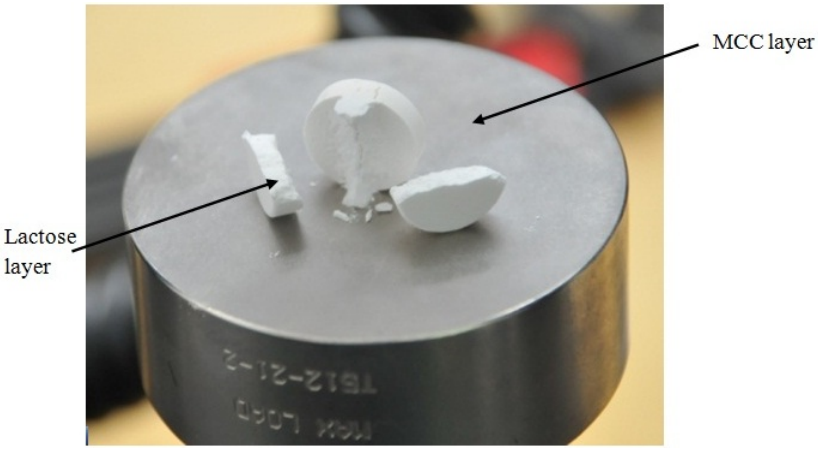

Fig. 16: Tablet after Brazilian Test.

CONCLUSIONS

Due to its behaviour upon compaction, MCC is proven to be elastically behaved while lactose possesses relatively plastic deformation behaviour. These behaviours of the powders also determine the diametrical fluctuations of the bi-layered tablet upon ejection. The mechanical integrity of the bi-layered tablets was also highly influenced by the powders characteristics. Under low compaction stresses the tablets produced does not undergo any form of deformation such as capping or lamination. However, tablets under these stresses have a lower mechanical integrity when it undergoes the Brazilian Test. For the tablets with higher compaction stresses, the tablets are found to be relatively strong to withstand higher load before cracking but usually experiences deformation during ejection mainly in the top layer of the tablet.

ACKNOWLEDGEMENT

Many thanks to the Department of Process and Food Engineering and Department of Mechanical and Manufacturing Engineering, Universiti Putra Malaysia, Serdang.

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