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Original article

EFFECTS OF COMPRESSION SPEED AND LUBRICATION ON THE COMPACTION PROPERTIES OF SOME COMMONLY USED DIRECT COMPRESSION MATERIALS

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Abstract

The purpose of this study was to investigate the effects of punch speed and lubrication (with and without the addition of 1% magnesium stearate) on the compaction properties of some commonly used commercial direct compression agents. The compressibility of these materials was analyzed using compression parameters derived from the Heckel equation. Three different classes of excipients having plastic, elastic and brittle fragmentation characteristics were evaluated, including microcrystalline cellulose (Avicel PH 101), pregelatinized starch (Starch 1500) and dibasic calcium phosphate (Fujicalin). Tablets were prepared using a compaction simulator under 20 kN force with a flat-faced 11mm punch. Three different speeds were investigated 10, 50 and 100 mm/sec. Data demonstrated that plastic materials like Avicel PH 101 form harder tablets at low compression speeds whereas brittle fragmenting materials like Fujicalin were relatively unaffected by compaction speed. Avicel PH 101 gave the hardest tablets at all compression speeds with and without the addition of lubricant.

Key words: *Compression speed, Lubrication, Avicel PH 101, Starch 1500, Fujicalin*

Basım Hızının ve Lubrikant Etkisinin Bazı Direkt Basım Ajanlarının Basım Özellikleri Üzerine Etkileri

Bu çalışmanın amacı, basım hızının ve lubrikasyonun (%1 magnezyum stearat ilave edilerek ve edilmeden) bazı ticari direkt basım ajanlarının basım özelliklerine etkilerini incelemektir. Bu materyallerin basılabilme özellikleri Heckel eşitliğinden elde edilen basım parametreleri yardımıyla analiz edilmiştir. Plastik, elastik ve kırılgan yapıya sahip olan üç farklı sınıftan eksipiyan; mikrokristal sellüloz (Avicel PH 101), prejelatinize nişasta (Starch 1500) ve dibazik kalsiyum fosfat (Fujicalin) değerlendirilmiştir. Tabletler 20 kN basınç ve 11 mm çapında zımba kullanılarak "compaction simulator" ile hazırlanmışlardır. Üç değişik hız incelenmiştir; 10, 50 ve 100 mm/s. Veriler, Avicel PH 101 gibi plastik yapıya sahip materyallerin düşük basım hızlarında dahi daha sert tabletler oluştururken Fujicalin gibi kırılgan yapıdaki materyallerin basım hızından etkilenmediğini göstermektedir. Avicel PH 101 ile basılan tabletler lubrikant eklenmesiyle ve eklenmemesiyle tüm basım hızlarında en sert tabletleri oluşturmuştur.

Anahtar kelimeler: *Basım hızı, Lubrikasyon, Avicel PH 101, Starch 1500, Fujicalin*

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INTRODUCTION

For many years, the rate of compaction has been known to have an effect on the compactability of materials (1-6). The consolidation of powder to form a dense compact requires deformation and an increase in interparticulate contact. Under compression, materials undergo complex stresses. This causes successive and simultaneous rearrangement, elastic and plastic deformation, fracture, the forming and breaking of interparticulate bonds (7). Materials undergoing plastic and/or viscoelastic deformation generally produce stronger tablets at reduced speeds, whereas brittle fragmenting materials are relatively unaffected by compaction speed because fragmentation occurs rapidly. Most powders, however, cannot be strictly categorized as exhibiting one type of deformation over another; usually a combination of deformation mechanisms exists. Materials that deform elastically or exhibit time-dependence are more susceptible to capping and lamination and/or strength reduction as the punch velocity is increased (5).

Several researchers (8,9) examined the effect of machine speed on the compaction behaviour of various directly compressible materials. The compact strength was found to be increased in lower machine speeds for viscoelastic materials such as pregelatinized starch and microcrystalline cellulose but it had minimal effect on brittle materials including dicalcium phosphate and lactose. They reported that an increase in powder bed density was dependent on the rate of force application (2,5). At higher speeds, the observed differences in crushing strength were due to an increase in the tablet porosity.

Lubricants are necessary additives in tablet formulations and magnesium stearate is one of the most commonly used lubricants (10). Makoto reported that magnesium stearate reduces tablet hardness and prolongs drug release and studies indicated that bulk drug powders and magnesium stearate interact with each other when thoroughly mixed before tablet compression (11). Vromans demonstrated that with a 0.5% magnesium stearate concentration, the mixing time does not have a significant influence on tablet hardness (12).

The aim of this study was to investigate the effects of both punch speed and lubrication (with and without the addition of 1%magnesium stearate) on the compaction properties of the some commonly used commercial direct compression agents (DTAs) especially to investigate and compare the compressibility properties of Fujicalin which is a new DTA with the other DTAs.

EXPERIMENTAL

The materials used were microcrystalline cellulose (Avicel PH 101, FMC Corporation, USA), pregelatinized starch (Starch 1500, Colorcon Ltd., England), anhydrous dibasic calcium phosphate (Fujicalin, Fuji Chemicals Ind. Co. Ltd., Japan), magnesium stearate (Pharma Ltd., USA).

True densities of Avicel PH 101, Starch 1500 and Fujicalin and with the addition of 1% magnesium stearate to these materials were measured with helium pycnometer (AccuPyc 1330, Micromeritics Instrument Inc., Norcross, GA). Calibration of the pycnometer was performed using a standard steel sphere before measurements. The experimental sample was accurately weighed and loaded into the sample cell. The sample volume was computed by measurements of the pressure observed by filling the sample chamber with ultra-high pure helium gas followed by discharging the gas into a second empty chamber. The measurements were repeated for 3 cycles.

Physical mixtures of each direct compression material with 1% magnesium stearate was performed with a cubic mixer for 5 minutes.

Compaction of 325 mg powder was carried out using a compaction simulator (Schmidt ServoPress 450), computer system (Schmidt PressControl 4000), amplifiers (Datalogging MPK, Kistler Type 5015) and software (HP 1702) fitted with a 11 mm flat-faced punch. The average compression rates were 10, 50 and 100 mm/s reflecting slow, medium and high compaction speeds respectively. The experiments were conducted under 20 kN force which was kept constant throughout the study.

The compaction data, which consisted of the forces on and the displacements of the upper and lower punches, were simultaneously collected. Subsequently, the acquired data were analyzed using the software (HP 1702) to obtain Heckel plots.

A computer programme was employed to fit data obtained during compaction to the Heckel Equation (Eq.1) (13,14)

$$ln\ (1/1-D) = K.P + A \qquad (1)$$

In Eq.1, **D** is the relative density of a tablet (the ratio of tablet density to true density of powder at applied pressure ***P***, ***K*** is the slope of the straight line portion of the Heckel plot and the reciprocal of ***K*** is the mean yield pressure. From the intercept of the linear portion of this plot, ***A***, the total densification of the powder bed due to die filling, was obtained.

Tablet dimensions were measured just after the compression and 24 hours later, with a micrometer and weights were determined on an analytical balance (Sartorius BP 211D). Hardness of the tablets were measured using a hardness tester (15).

RESULTS AND DISCUSSION

True densities of Avicel PH 101, Starch 1500 and Fujicalin and with the addition of 1% magnesium stearate to these materials were given in Table 1. Comparing the true densities of these commercial direct compression agents, the true density results are quite close to each other with the exception of Fujicalin.

Table 1. True density results of the materials

Sample	True density ±SD (g/ml)
Avicel PH 101	1.58±0.0004
Fujicalin	2.89±0.0004
Starch 1500	1.50±0.0012
Avicel PH 101+ 1%magnesium stearate	1.57±0.0002
Fujicalin+ 1%magnesium stearate	2.83±0.0026
Starch1500+1%magnesium stearate	1.49±0.0032

Table 2 shows the hardness results of the tablets. The effect of compression speed or punch velocity on compacts has been reported by David and Augsberger (16). They studied the duration of the overall compression cycle on the tablet strengths of the direct compression excipients lactose, direct compressible sugar, microcrystalline cellulose (MCC) and compressible starch. They observed that an increase in the duration of the overall compression cycle from 0.09 to 10 seconds resulted in significant increases in the tensile strengths of tablets prepared from MCC and compressible starch fillers, but not with lactose or compressible sugar. This was attributed to differences between the extent of plastic flow of MCC or compressible starch. Rees (17), confirmed that the strengths of perfectly elastic-brittle particles showed no compression rate dependence whereas visco-elastic particles, capable of plastic deformation, manifested changes in strengths with compression speeds.

Zhang et al. reported that hydrogen bonding plays a big role in compaction hardness of Avicel PH 101. Hydrogen bonding is important because Avicel PH 101 undergoes significant plastic deformation during compression bringing an extremely large surface area into close contact and facilitating hydrogen bond formation between the plastically deformed, adjacent cellulose particles. In addition, the existence of moisture within the porous structure of Avicel PH 101 acts as an internal lubricant. This facilitates slippage and flow within the individual microcrystals during plastic deformation, which enforces the formation of hydrogen bond bridges and gives Avicel PH 101 a very good hardness (18).

Table 2. Hardness values of the tablets (n=6, values are in Newton)

Speed / Material	**10mm/sec (Mean±SD)**	**50mm/sec (Mean±SD)**	**100mm/sec (Mean±SD)**
Avicel PH 101	387.17±27.48	414.33±15.00	396.83±25.54
Fujicalin	97.83±12.82	101.33±5.05	82.17±10.03
Starch 1500	52.50±9.03	38.00±2.37	36.00±3.16
AvicelPH101+ 1% magnesium stearate	239.00±1.90	228.00±14.30	216.50±4.35
Fujicalin+ 1%magnesium stearate	90.45±25.66	102.67±7.63	102.67±8.80
Starch1500+ 1%magnesium stearate	Tablet formation did not occur	Tablet formation did not occur	Tablet formation did not occur

It is commonly known that the stresses leading to capping are most likely to develop during the unloading phase of compaction, during which the expansion of elastically deformed particles ruptures interparticulate bonds (5). It has also been reported that capping tendency increases with increasing rates of decompression (19). Although microcrystalline cellulose used for this study did not display lamination under 20 kN force at 100 mm/sec speed but Celik and Okutgen observed capping/lamination of microcrystalline cellulose at approximately 300 MPa for 300mm/sec. speed. They found microcrystalline cellulose to be even more prone to capping when the punch speed was increased to 600 mm/sec, resulting in significant reductions in crushing strength values as the pressure was increased (20).

Fujicalin is found to exhibit poor binding properties. Because of its brittle nature, it is thought that it undergoes considerable fragmentation during compression. Fracture creates a large number of interparticulate contact points, which imply that a comparetively weak type of bonding is involved (21). Thus, the compact strength is low when compared with Avicel PH 101.

Starch compacts generally have low hardness (18). It was reported that in comparison with other plastically deforming materials, such as MCC, the plastic deformation of starch during compression is too slow to produce adequate interparticle binding during rapid compression. Compression of Starch 1500 at all compression speeds, even at the lowest compression speed produced weak tablets with a high tendency to cap.

Hardness values were found in agreement with the literature findings. It is observed that addition of lubricant facilitates slippage and flow properties for Avicel PH 101 and Fujicalin, and resultants with sufficent compact strength. On the contrary, addition of 1% magnesium stearate to Starch 1500, tablet formation did not occur because of its plastic behavior under pressure, Starch 1500 is observed to be extremely sensitive to mixing with magnesium stearate. Manudhane et al. reported that after mixing Starch 1500 with 0.5 % magnesium stearate in a Turbula mixer at 90 rpm, the tablet crushing strength decreased from 18 kg down to zero within 10 minutes. For this reason, the use of alkaline stearates should be avoided or kept below 0.25 % for Starch 1500 (22).

Even when filling the material into the die is carried out manually at constant weight and not considering flow properties of materials, a significant source of error can be made on the compacted mass measurement. The weight of the compact obtained after ejection may differ from the real weight of the product compacted because of the sticking to punches and die walls, capping, lubrication of the die etc. However, for products which are easily compressed like drug products and direct compression excipients, the weight error may be lower (4). In order to minimize weight errors, a constant weight (325 mg) of powder mass was maintained for all samples.

Initial and t= 24 hour weight and thickness results for different speeds are shown in Tables 3-5. Most tablets need 24 hours to fully settle from the compression and ejection events (23).

Table 3. Mean±SD thickness (mm) and weight (mg) results of Avicel PH 101 and Avicel PH 101+ 1% magnesium stearate tablets for different speeds (mm/sec).

	Avicel PH 101			**Avicel PH 101+1%Magnesium stearate**		
	10mm/sec	**50mm/sec**	**100mm/sec**	**10mm/sec**	**50mm/sec**	**100mm/sec**
initial thickness t=0	2.335±0.009	2.391±0.017	2.323±0.024	2.348±0.013	2.403±0.025	2.409±0.030
thickness t=24 hours	2.369±0.009	2.412±0.017	2.346±0.024	2.394±0.014	2.437±0.023	2.449±0.030
initial weight t=0	315.830±1.610	318.662±2.032	310.798±2.350	316.09±1.432	318.052±1.196	318.392±3.389
weight t=24 hours	317.858±1.457	319.603±1.796	311.967±2.378	318.49±1.446	319.627±1.168	320.447±4.193

Table 4. Mean±SD thickness (mm) and weight (mg) results of Starch 1500 tablets for different speeds (mm/sec).

	Starch 1500		
	10mm/sec	**50mm/sec**	**100mm/sec**
initial thickness t=0	2.633±0.036	2.684±0.020	2.747±0.018
thickness t=24 hours	2.730±0.035	2.803±0.019	2.838±0.021
initial weight t=0	317.595±4.488	319.248±1.126	319.462±1.122
weight t=24 hours	320.085±4.408	323.267±1.1872	322.184±1.215

Yield pressure values for Heckel plots of excipients with and without lubricant (1% magnesium stearate) for different punch speeds evaluated in this study are displayed in Table 6 and Heckel profiles are shown in Figures 1-10. The slope of the Heckel plot gives a measure of the plasticity of a compressed material and the reciprocal of *k* is known as the yield value (P_y). Yield value reflects the deforming ability of the material. The soft, ductile powders have lower yield value. The agglomerates with low yield value could be plastically deformed as a result of rebonding of smaller primary crystals. Low value of P_y (steep slope) reflects low resistance to pressure, good densification and easy compression. A large value of slope indicates the onset of plastic deformation at relatively low pressure (24).

In regard to the yield value results of the investigated compression materials, it is observed that Starch 1500 have an intermediate behaviour between totally plastic and brittle products.

Table 5. Mean±SD thickness (mm) and weight (mg) results of Fujicalin and Fujicalin + 1% magnesium stearate tablets for different speeds (mm/sec).

	Fujicalin			Fujicalin+1%Magnesium stearate		
	10mm/sec	**50mm/sec**	**100mm/sec**	**10mm/sec**	**50mm/sec**	**100mm/sec**
initial thickness t=0	1.871±0.021	1.874±0.006	1.904±0.011	1.869±0.014	1.861±0.021	1.853±0.024
thickness t=24 hours	1.894±0.023	1.897±0.007	1.920±0.009	1.886±0.010	1.882±0.023	1.869±0.024
initial weight t=0	316.422±3.746	318.323±2.818	315.247±4.956	322.770±1.215	321.352±1.214	321.443±0.756
weight t=24 hours	316.513±3.950	319.157±3.676	315.682±5.258	322.262±0.986	321.957±1.224	321.56±0.787

Table 6. Yield pressure values for the studied excipients at compression speeds of 10, 50 and 100 mm/s.

Excipient	Yield pressure (MPa)					
	with lubricant (1% magnesium stearate)			**without lubricant**		
	10mm/s	**50mm/s**	**100mm/s**	**10mm/s**	**50mm/s**	**100mm/s**
AvicelPH 101	40.3	46.2	50.7	42.0	48.4	51.7
Starch 1500	-	-	-	39.2	44.4	50.1
Fujicalin	38.6	39.7	39.9	41.7	42.6	44.0

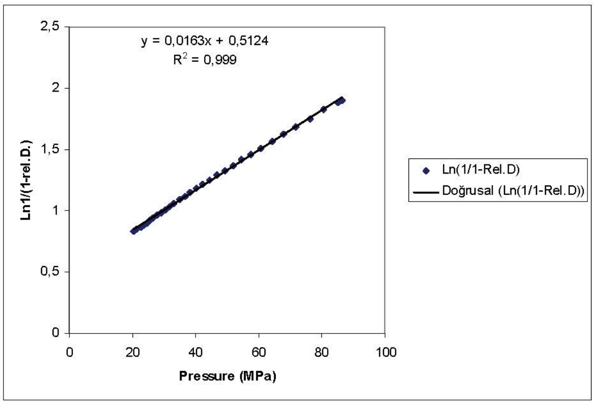

Figure 1. Heckel plot for Avicel PH 101 at a compression speed of 10 mm/sec

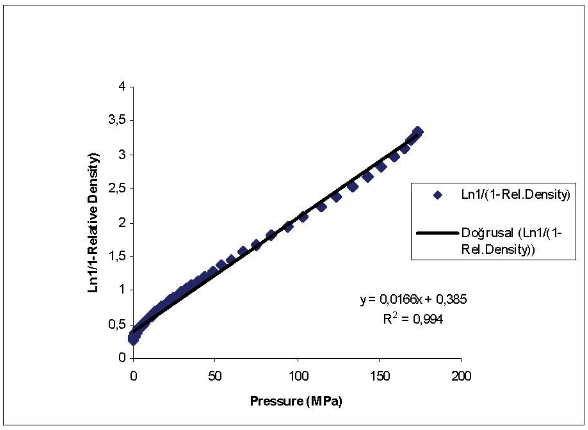

Figure 2. Heckel plot for Avicel PH 101 at a compression speed of 50 mm/sec.

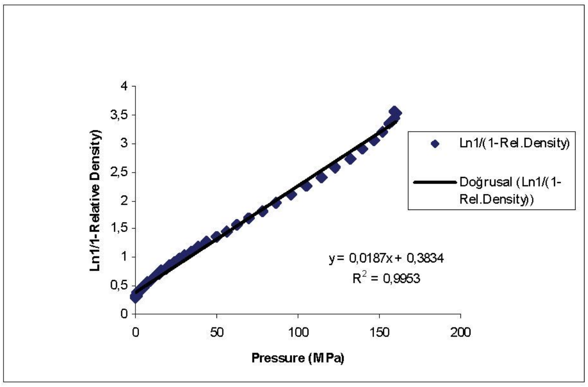

Figure 3. Heckel plot for Avicel PH 101 at a compression speed of 100 mm/sec.

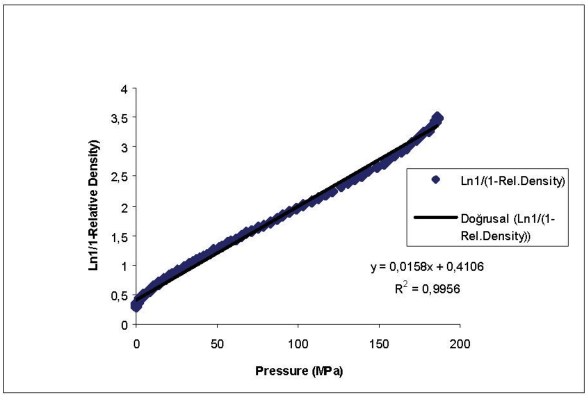

Figure 4. Heckel plot for Avicel PH 101 containing 1% magnesium stearate at a compression speed of 100 mm/sec.

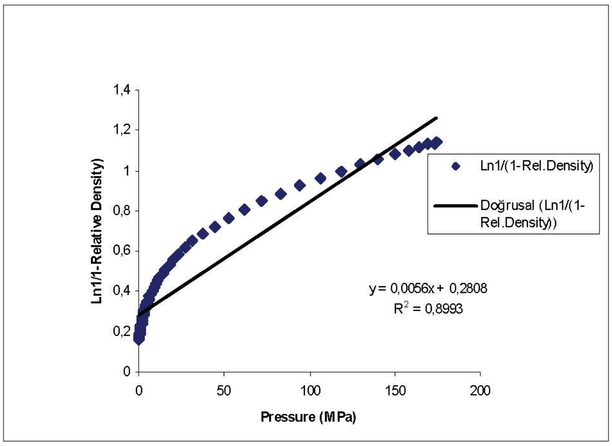

Figure 5. Heckel plot for Fujicalin at a compression speed of 50 mm/sec.

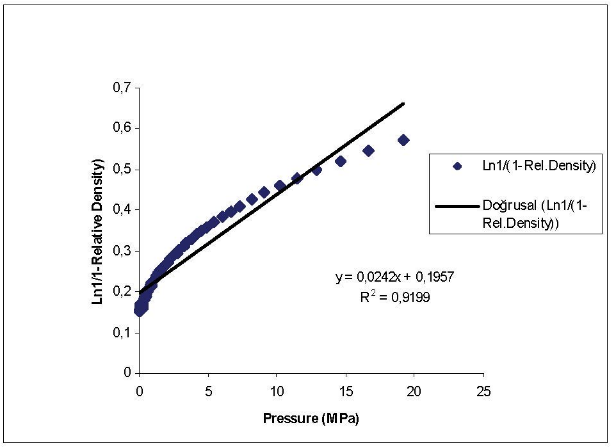

Figure 6. Heckel plot for Fujicalin containing 1% magnesium stearate at a compression speed of 50 mm/sec.

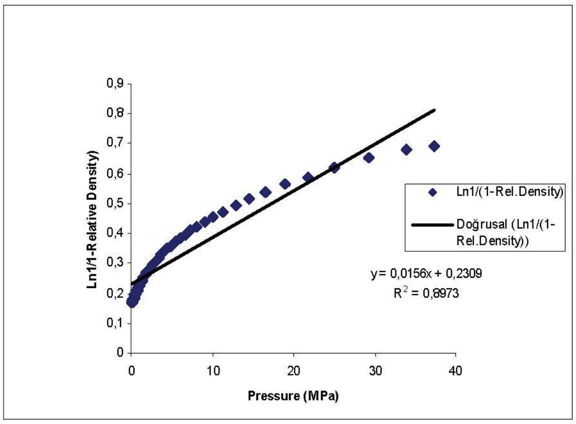

Figure 7. Heckel plot for Fujicalin containing 1% magnesium stearate at a compression speed of 100 mm/sec.

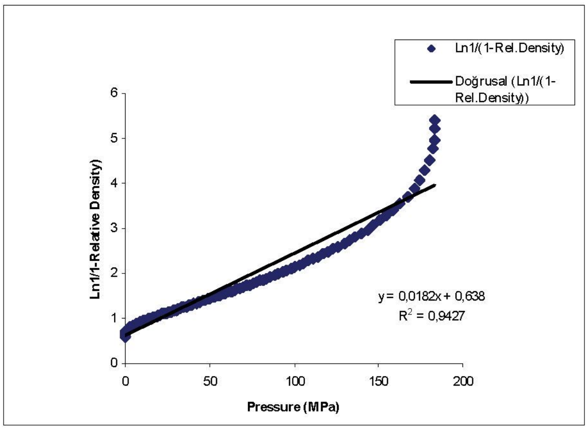

Figure 8. Heckel plot for Starch 1500 at a compression speed of 10 mm/sec.

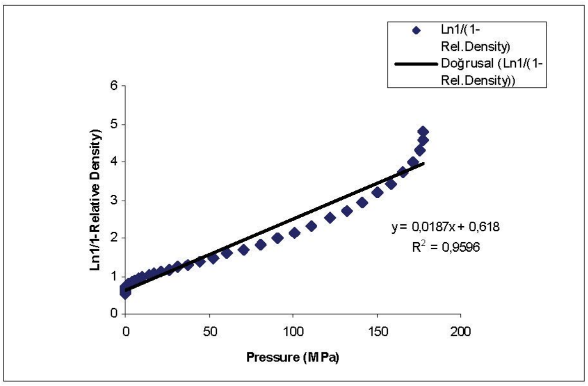

Figure 9. Heckel plot for Starch 1500 at a compression speed of 50 mm/sec.

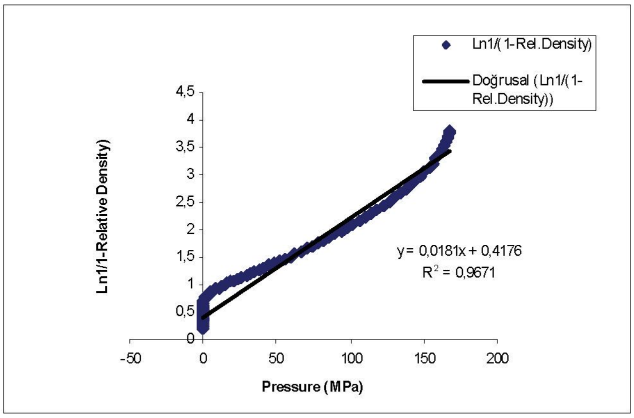

Figure 10. Heckel plot for Starch 1500 at a compression speed of 100 mm/sec.

During compaction, MCC is thought to undergo stress relief deformation by several mechanisms. It is reported that at low compression forces, stress relief is dominated by a slight elastic phase. At higher force, there is either further deformation or permanent deformation by nonspecific plastic flow (21).

It is found that the yield pressure increases with punch velocity, because of a reduction in the amount of plastic deformation caused by time-dependent nature of plastic flow. This increase in mean yield pressure at increasing compression speeds. The reduction in crushing strength at increasing compression speed is caused by an increased porosity of the compacted powder bed (21).

The strength of Starch 1500 tablets are found to be low. This effect may be because plastic deformation is too slow to produce adequate interparticle binding during rapid compression. Compaction at high speeds, a large proportion of the total deformation is thought to be elastic. Interparticle bonds are not formed rapidly enough to prevent brittle fracture.

As expected, Fujicalin showed minimal stress relaxation. Because of its brittle nature, the tensile strength of Fujicalin tablets hardly affected by an increase in tableting speed. As compared other fillers and binders, the binding properties of Fujicalin are moderate which is an effect of its brittle nature. It is observed that magnesium stearate has no effect on its binding properties. This effect can be explained by the assumption that clean, lubricant free surfaces created by fragmentation of Fujicalin during the process of consolidation and compaction.

CONCLUSION

Data demonstrated that plastic materials like Avicel PH 101 form harder tablets at low compression speeds whereas brittle fragmenting materials like Fujicalin were relatively unaffected by compaction speed. Avicel PH 101 gave the hardest tablets at all compression speeds with and without the addition of lubricant. It is confirmed that because of its plastic deformation under pressure, Avicel PH 101 perform as a binder whereas both fragmentation and plastic deformation take place in Starch 1500.

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