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# Hexagonal boron nitride as a tablet lubricant and a comparison with conventional lubricants

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**Abstract**

The objective of this study was to investigate the lubrication properties of hexagonal boron nitride (HBN) as a new tablet lubricant and compare it with conventional lubricants such as magnesium stearate (MGST), stearic acid (STAC), and glyceryl behenate (COMP). Tablets were manufactured on an instrumented single-station tablet press to monitor lower punch ejection force (LPEF) containing varied lubricants in different ratio (0.5, 1, 2%). Tablet crushing strength, disintegration time and thickness were measured. Tensile strength of compacted tablets were measured by applying a diametrical load across the edge of tablets to determine mechanical strength. The deformation mechanism of tablets was studied during compression from the Heckel plots with or without lubricants. MGST was found to be the most effective lubricant based on LPEF—lubrication concentration profile and LPEF of HBN was found very close to that of MGST. HBN was better than both STAC and COMP. A good lubrication was obtained at 0.5% for MGST and HBN (189 and 195N, respectively). Where COMP and STAC showed 20 and 35% more LPEF compare to that of MGST (239 and 288N, respectively). Even at the concentration of 2% COMP and STAC did not decrease LPEF as much as 0.5% of MGST and HBN. Like all conventional lubricants the higher the concentration of HBN the lower the mechanical properties of tablets because of its hydrophobic character. However, this deterioration was not as pronounced as MGST. HBN had no significant effect on tablet properties. Based on the Heckel plots, it was observed that after the addition of 1% lubricant granules showed less plastic deformation.


*Keywords:* Lubricants; Hexagonal boron nitride; Tablets; Lower punch ejection force (LPEF); Magnesium stearate

## 1. Introduction

It is rare to find a solid oral dosage product consisting of drug alone. To produce a final product that is not only practical and convenient to handle but also facilitates patient compliance, the drug substance needs to be processed with other excipients. The drug "fillers" or "excipients" serve many purposes in the formulation. One class of functional excipients that is essential in the most tablet formulations is "lubricants". Lubricants are pharmaceutical excipients that decrease friction at the interface between a tablet surface and the die wall during ejection and reduce wear on punches and dies, prevent sticking to punch faces, improve the fluidity and filling properties and manufacturing efficiency of solid preparations. Insufficient fluidity of the bulk powder in the tabletting process causes problems such as an increase in the variability of the tablet weight, impairment of content uniformity and deterioration of the product quality. Also, inadequate plasticity due to friction and adhesion among powder particles lead to troubles in the manufacturing process and deterioration of productivity (Aoshima et al., 2005). Friction can also damage the machine and tablets during ejection. Moreover, high temperature generated during compression can affect drug stability (Kara et al., 2004). In order to minimize these problems it has been usual to incorporate a lubricant in small quantities in the powder or granules to be tabletted. An ideal lubricant should act by reducing shear strength at the interface between the tablet and die wall, reducing the coefficient of friction and hence the frictional force at a given load, it should be non-toxic, chemically inert, unaffected by process variables, have no adverse effects on the finished dosage form, and be consistent from batch to batch (Miller and York, 1988; Velasco and Rajabi-Siahboomi, 1998). A wide range of lubricants are available for pharmaceutical applications. Some of the commonly used tablet lubricants are magnesium stearate (MGST), stearic acid (STAC), glycerol esters of fatty acids, DL leucine and sodium benzoate (Turkoglu et al., 2005). Hexagonal boron nitride (HBN) is an interesting

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compound with the potential of being used as a tablet lubricant to be incorporated into tablet formulations. HBN is one of the two common crystalline structures of boron nitride (BN). These structures are cubic and hexagonal. Cubic boron nitride (CBN) is like diamond, being hard and abrasive (Lipp et al., 1989). Hexagonal boron nitride is like graphite being soft and lubricious. This inorganic solid powder retains its ability to lubricate in extreme cold or heat and is well suited to extreme pressure applications. HBN is highly heat stable material. It is typically synthesized from boric oxide or boric acid in the presence of urea or urea derivatives and ammonia at temperatures ranging from 800 to 2000 °C. HBN has a density of 2.27 g/cm$^3$ and melting point of 3000 °C and it shows a high thermal conductivity comparable to that of stainless steel (Kalyoncu, 1985). In addition, it is an inert material that will not react with other pharmaceutical excipients during manufacturing. When used as a high purity material such as 99.9%, it can be considered as safe. Based on a report issued by the National Toxicology Program (Baraton et al., 1993) no evidence exist that boron nitride, boric acid or boric oxide are carcinogens or pose any toxic hazard nor are any of these materials considered hazardous by the International Agency for Research on Cancer, The Occupational Safety and Health Administration (OSHA) or the American Conference of Government and Industrial Hygienists (ACGIH, 1994/1995). Boron nitride, boric acid or boric oxide are not considered hazardous chemical under EPA or SARA guidelines and no regulations exist regarding their use, transport or disposal. While some references prior to 1970 cite toxicity hazards associated with boron, more recent studies do not support earlier claims and references indicate that previously reported effects of boron are inaccurate (Lelonis et al., 2003). In any case, high purity, commercial grade HBN powders typically do not contain free boron. All boron is either in the form of a nitride or borate.

The most commonly studied lubricant is MGST. The lubrication properties of MGST vary from batch to batch even when the material is obtained from the same producer. It was also reported that crystalline structure, particle size, and fatty acid composition affect its lubrication properties (Leinonen et al., 1992). Extended mixing time and the use of higher concentrations of MGST, such as more than 1% may cause many problems during and after tablet manufacturing. In particular, there have been a number of studies concerning a delay of tablet disintegration time. The delay of disintegration of tablets due to MGST has been shown to affect the bioavailability of the active ingredients (Flores et al., 2000; Eissen et al., 2002). The decrease of tablet crushing strength with the increasing MGST levels (Mollan and Çelik, 1996), and with the extended mixing time (Shah and Mlodozeniec, 1977) were well demonstrated in literature.

Undoubtedly, the best method to omit the drawbacks of the lubricant in a tablet formulation is to apply alternative lubrication methods, mostly involving modifications of tablet machines. Kara et al. (2004), investigated possible use of zirconia as a material for the manufacture of punches and dies for use in tablet machines and to study its effect on ejection of tablets made from different formulations. They found that zirconia was an alternative to stainless-steel tooling. The addition of exact amount of suitable lubricant directly on to punch and die surfaces immediately after tablet ejection has also been reported (Staniforth et al., 1989; Laich and Kissel, 1997). The effectiveness of tablet lubricants, which requires providing a decrease in the lower punch ejection force (LPEF) and the relation of lubricant properties with the mechanical strength of the tablets was often reported in the literature (Delacourte et al., 1993; Röscheisen and Schmidt, 1995).

This study is the second application of HBN as a tablet lubricant. In the previous study carried out by Turkoglu et al. (2005) lower punch ejection force was calculated by comparing the ejection force of control batches with those of lubricant containing ones. However, in this study LPEF values was calculated quantitatively using Labview software (Version 7.1). This study evaluates HBN as a new tablet lubricant and compares its properties with MGST, STAC, and glyceryl behenate (COMP).

## 2. Materials and methods

### 2.1. Materials

Avicel PH 102 was donated FMC, Brussels, Belgium. Lactose Monohydrate Ph.Eur./USP-NF/JP was obtained from Meggle AG, Wasserburg, Germany. Povidone K30 was a gift from BASF, Ludwigshafen, Germany. MGST, STAC, Compritol 888 and HBN were obtained from Mallinckrodt, St. Louis, MO, USA; Sherex, Dublin, OH, USA; ATO, Gattefose, Cedex, France; ITU, High Technology Ceramics and Composites Research Center, Istanbul, Turkey, respectively.

### 2.2. Methods

#### 2.2.1. Instrumentation of tablet press

A single-station tablet press (Korsch EKO, Berlin, Germany) was instrumented for monitoring upper and lower punch forces. Compression and ejection forces were monitored, recorded, and interpreted continuously during tablet manufacturing. Two ring-type ICP® Dynamic Force Sensors (Model 203B for upper punch, and 201B03 for lower punch, PCB Piezotronics, Inc. Depew, NY, USA) were used to detect compression and ejection force input signals. Each sensor was connected to a signal conditioner (Model 480E06, PCB Piezotronics, Inc.) with a standard sensor cable. ICP signal conditioner offers amplification factors of 1, 10, and 100. The output signal was transferred to an analog-digital converter board (PCI 6023E, National Instruments Austin, TX, USA) and finally the analog-digital converter was connected to a PC. Using PC-based software (National Instruments, NI-DAQ, Labview, Version 7.1, Austin, TX, USA) the output signal was transferred time *vs*. voltage front panel graph continuously. Block diagram of software and schematic diagram of instrumentation are also seen in Figs. 1 and 2. Finally, upper punch compression and lower punch ejection forces were determined quantitatively with this system.

#### 2.2.2. Preparation of granules and tablets

750 g microcrystalline cellulose (Avicel PH102) and 750 g Lactose Monohydrate were mixed for 10 min, to this mixed powder, 250 g of a aqueous solution of 45 g of povidone K30 was

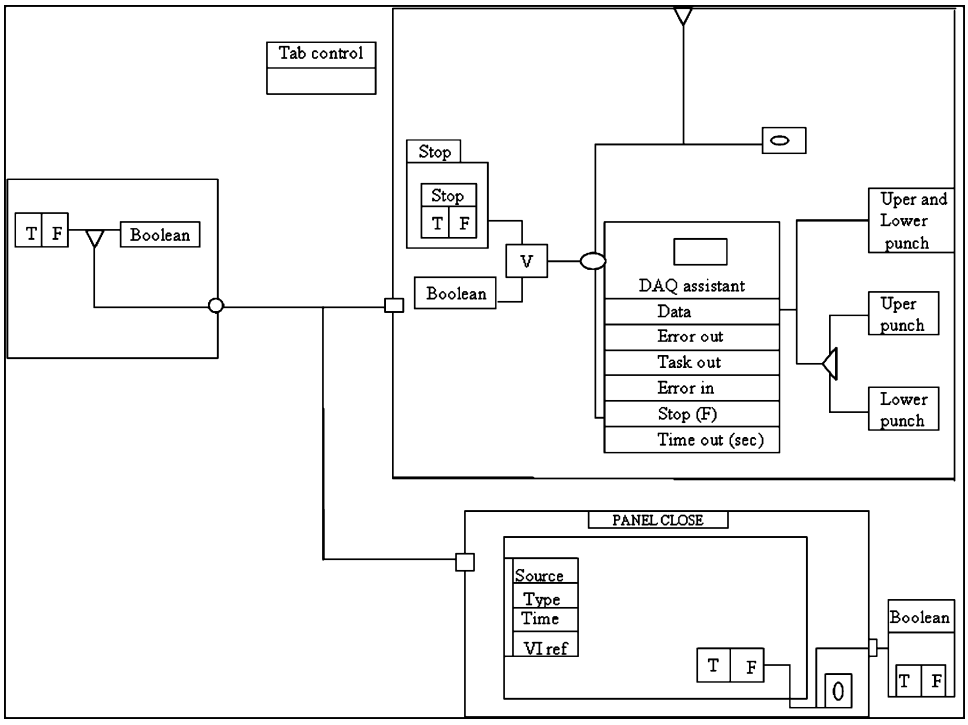


Fig. 1. This is the illustration of block diagram of front panel. This program was written by the help of National Instruments, NI-DAQ, Labview, Version 7.1 software. Using this program detected output signal was transferred to time *vs*. voltage front panel. Finally, upper punch compression and lower punch ejection force (LPEF) were determined.

added and the mixture was mixed for another 20 min. Wet granules were sieved through 2 mm screen and dried overnight at 45 °C. After drying, dry granules were sieved through 0.8 mm screen to make master granule formula. All lubricants were added to the 100 g of master granule formula, depending on their studied concentrations and mixed in a V-blender for 5 min. For lubricant performance, 12 batches of tablets were manufactured using the instrumented tablet press with a 9 mm flat faced punch set. Study design is seen in Table 1.

### 2.2.3. Determination of upper punch compression force and lower punch ejection force

Using four different lubricants and three different concentrations a total of 12 batches were compressed using instrumented and PC-connected tablet press. To determine upper punch compression force and LPEF quantitatively, a 235 mg lubricated granule was weighed precisely and placed into the die of tablet press then tablets were compressed. Ten replicates were done and signals were detected. The signal was received as voltage (V) from the force sensor. The sensors produced a signal between ±5 V.

### 2.2.4. Measurement of the tablet properties

The weight variation of tablets was determined according to the USP24. Tablet diameter and thickness were measured using a micrometer with a sensitivity of 0.01 mm (Bestool-Kanon, Japan). The diametrical tablet crushing strength was evaluated using a tablet hardness tester (Model C50, I Holland, Ltd., Nottingham, UK). The disintegration time of tablets were evaluated according to the USP 24.

### 2.2.5. Tensile strength measurement of tablets

Tensile strength of tablets can generally be determined by diametrical compression tests, considering the actual tablet from a right circular cylinder (Fell and Newton, 1970). In the diametrical compression tests, cylindrical tablets were placed between

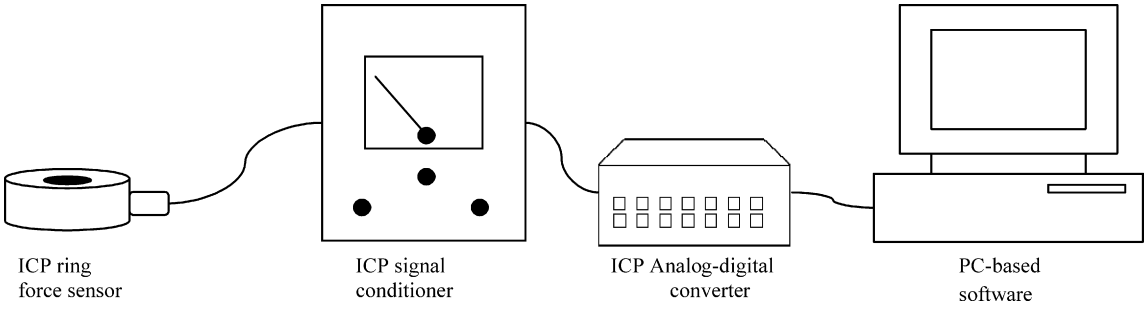


Fig. 2. Schematic diagram of instrumentation.

two platens and compressed diametrically until the tablets break/crush. The compression force ($F$) needed to fracture the tablets along their diameter was determined in a tablet hardness tester (Model C50, I Holland, Ltd.). The tensile strength of the tablets ($\sigma$) was calculated based on an equation (Fell and Newton, 1970).

$$\sigma = \frac{2F}{\pi Dt} \quad (1)$$

$F$ is applied force, $D$ is the tablet diameter and $t$ is the tablet thickness.

### 2.2.6. Compression behavior of tablets

The compression properties of lubricated and unlubricated formulations were characterized by using the Heckel plots (Heckel, 1961a,b). The Heckel equation is widely used in pharmaceutical formulation and is an expression of volume reduction properties of the powders which was evaluated by the porosity of the compact *vs*. the pressure of compaction (Pontier et al., 2002).

$$\ln\left(\frac{1}{1-D}\right) = kP + A \quad (2)$$

where $D$ is the relative density of a powder column at the compression pressure $P$. $K$ and $A$ are constant (Heckel, 1961a,b). Porosity is a function of the voids in a powder column, including both inter and intra particulate voids. For porosity measurement, the dimensions and weight of a powder column (i.e. apparent density) and the particle density of solid material should be known. The porosity, $\epsilon$ can be expressed by the equation

$$\epsilon = \frac{1-\rho_A}{\rho_T} \quad (3)$$

where $\rho_A$ is the apparent density of a powder column, and $\rho_T$ is the true density. The value of $\rho_A/\rho_T$, also referred as $D$, is regarded as the relative density (Kuny, 2004). Usually, the volume of the entire tablet, $V_A$ is calculated from the measured height and the area of the compact. The determination of these dimensions is normally done when the compression is finished and the tablet is ejected. This kind of measurement is called zero-pressure determination. The so-called apparent density $\rho_A$ is determined by division of the tablet weight "$m$" by the apparent volume, $V_A$. The relative density $\rho_r$ is obtained by dividing the apparent density by the true density:

$$\rho_r = D = \frac{\rho_A}{\rho_T} = \frac{V_T}{V_A} \quad (4)$$

The parameter $V_T$ characterizes the true volume of the solid particles and therefore Eq. (4) shows that the relative density is essentially a solid fraction. This volume fraction, which is occupied by the solid, is linked to the volume fraction of the voids, i.e. the porosity, $\varepsilon$ (Kuny, 2004).

$$\epsilon = \frac{(V_A - V_T)}{V_A} = 1 - \left(\frac{V_T}{V_A}\right) = 1 - \rho_r = 1 - D \quad (5)$$

To determine compression properties of lubricated and unlubricated formulations 756 mg of the corresponding mixtures were compressed at nine different compaction pressures in a laboratory type hydraulic press up to 53 MPa (3.3, 6.6, 13.3, 19.9, 26.5, 33.2, 39.8, and 46.5 MPa). The punches used were flat and had a diameter of 13 mm. The selected compaction pressures were maintained for 10 s to allow the development of most possible plastic deformation on the powders, to avoid the effect of different dwell times producing different degrees of deformation. The thickness of tablets was measured and volume of tablets was calculated to find volume reduction.

Table 1
Study design

| Formulation | Lubricant type | Lubricant concentration (%) |
|---|---|---|
| F1 | MGST | 0.5 |
| F2 | MGST | 1 |
| F3 | MGST | 2 |
| F4 | HBN | 0.5 |
| F5 | HBN | 1 |
| F6 | HBN | 2 |
| F7 | COMP | 0.5 |
| F8 | COMP | 1 |
| F9 | COMP | 2 |
| F10 | STAC | 0.5 |
| F11 | STAC | 1 |
| F12 | STAC | 2 |

Mixing time: 5 min.

## 3. Results and discussion

### 3.1. Tablet preparation and determination of upper punch compression force and LPEF

Study design is summarized in Table 1. Trials were made with 3 levels of (0.5, 1, and 2%) MGST, HBN, COMP, and STAC. Without any lubricant jamming of lower punch observed dur-

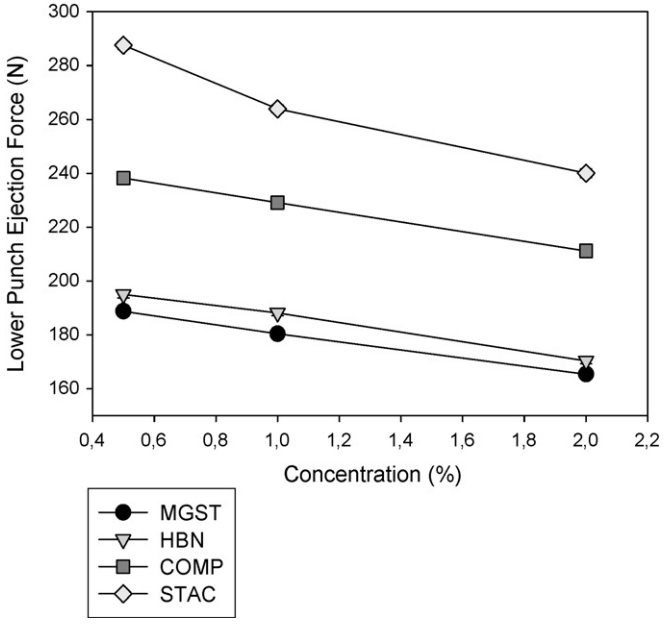


Fig. 3. Concentration *vs*. LPEF graph of the lubricants.

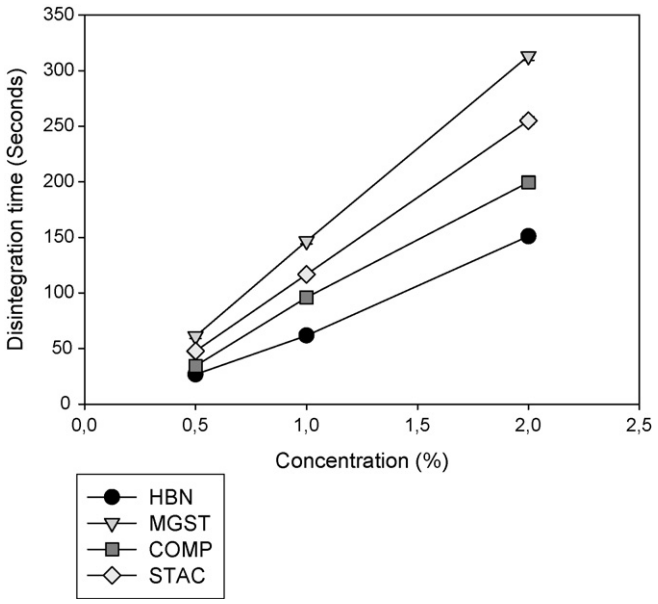


Fig. 4. Concentration *vs.* disintegration time of tablet containing various lubricant.

ing compression of the tablets. Therefore, unlubricated granule formulation was not given in this study. Jamming was observed because of the high concentration of PVP K30 in the studied granule. Granules were filled into the die of the punches manually and 10 perpetual compressions were made and the average of the data were calculated. Tablet weight and upper punch compression pressure (8.5 kN) were kept constant to prevent any variation from compression procedure. Granule fluidity can be enhanced with increasing lubricant concentration. Any change in the granule fluidity causes to tablet weight variation (Shah and Mlodozeniec, 1977; Aoshima et al., 2005). The LPEF is the most direct measurement to show effectiveness of a lubricant. Therefore, Fig. 3 presents the most reliable evaluation of the

Table 2
Tensile strength variation of tablets including different lubricants (MPa)

| Concentration (%) | MGST | HBN | COMP | STAC |
|---|---|---|---|---|
| 0.5 | 2.44 ± 0.18 | 2.47 ± 0.21 | 2.55 ± 0.17 | 2.52 ± 0.23 |
| 1 | 1.87 ± 0.28 | 2.19 ± 0.21 | 2.33 ± 0.27 | 2.01 ± 0.25 |
| 2 | 1.34 ± 0.19 | 1.85 ± 0.25 | 2.08 ± 0.16 | 1.65 ± 0.17 |

lubricant activity. Magnesium stearate is the most widely used lubricant in tablet manufacturing and it was used as a reference. No jamming observed with the three levels of selected lubricant. LPEF values decreased with increase in lubricant concentration. At 0.5% level HBN and MGST were found to be more effective lubricants and they showed the highest lubricant efficiency, 189 and 195N, respectively. Where COMP and STAC showed 20 and 35% more LPEF compare to that of MGST (239 and 288N, respectively). Even at the concentration of 2% COMP and STAC did not decrease the LPEF as much as 0.5% of MGST and HBN. Results obtained in this study on LPEF data comply with that of Turkoglu et al. (2005).

### 3.2. Evaluation of tablet properties

Fig. 4 shows the relationship between the lubricant concentration and disintegration time of tablets. One of the undesirable side effects of lubricant addition to pharmaceutical formulation is the prolongation of tablet disintegration times. Among the studied lubricants disintegration is delayed more markedly as the MGST concentration is increased (Durig and Fassihi, 1997). The disintegration time with MGST was found to be 313 s, which was longer than those with the other lubricants and was related to its concentration. The disintegration time was 61, 147, and 313 s for MGST at 0.5, 1, and 2% concentration, 27, 62, and 151 s for HBN, 34, 96.5, and 199.3 s for COMP and 48, 117, and 255 s for STAC, respectively. MGST delays the disintegration of tablets by forming a hydrophobic membrane on the surface of granule

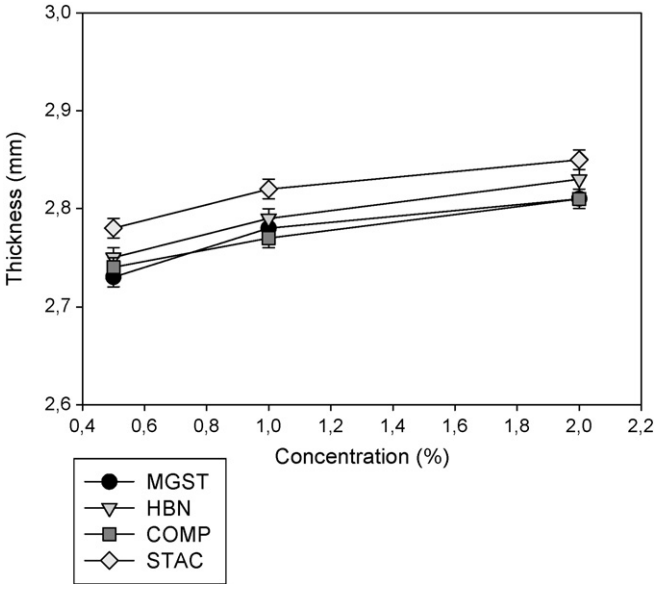


Fig. 5. Concentration *vs.* thickness of tablet containing various lubricant.

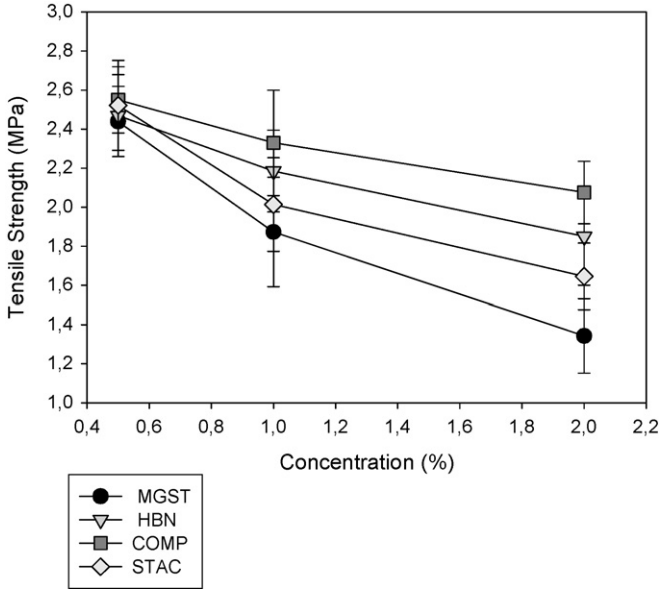


Fig. 6. Concentration *vs.* tensile strength of tablet containing various lubricant.

Table 3
Data of lubricated and unlubricated granules

| Pressure (MPa) | ln (1/porosity) data | | | | |
|---|---|---|---|---|---|
| | Granule | Granule + MGST | Granule + HBN | Granule + COMP | Granule + STAC |
| 46.5 | 4.247 | 3.490 | 3.650 | 3.849 | 3.352 |
| 39.8 | 3.417 | 3.126 | 3.175 | 3.229 | 2.986 |
| 33.2 | 3.073 | 2.827 | 2.861 | 2.941 | 2.758 |
| 26.5 | 2.574 | 2.475 | 2.496 | 2.522 | 2.427 |
| 19.9 | 2.224 | 2.141 | 2.156 | 2.189 | 2.095 |

particles. The least pronounced effect was observed with HBN at 2% lubricant concentration. HBN was found to be an effective lubricant, in addition, not having a negative effect on tablet disintegration times even at 2% level was considered to be an advantage with this material. The results complied with Durig and Fassihi (1997), Aoshima et al. (2005) and Turkoglu et al. (2005).

Changing in tablet porosity against lubricant concentration is shown in Fig. 5. At 0.5% lubricant concentration the tablet thickness were found to be 2.73, 2.75, 2.74, and 2.78 mm for MGST, HBN, COMP, and STAC, respectively. At 2% lubricant concentration tablet thickness values increased to 2.81, 2.83, 2.81, and 2.85 mm with MGST, HBN, COMP, and STAC. Tablet thicknesses increased proportionally with increasing lubricant concentration.

### 3.3. Evaluation of tensile strength of tablets

Tensile strength and porosity of the tablets are macroscopic properties that however reflect the structure of the tablet on microscopic levels. Fig. 6 and Table 2 show lubricant *concentration vs. tensile strength*, where all studied lubricants depending on their concentration lowered tablet tensile strength. At a concentration of 0.5% the tensile strength of tablets including MGST, HBN, COMP and STAC were 2.44, 2.47, 2.55, and 2.52 MPa, respectively. When the concentration of lubricant increased at a level of 2%, the tensile strength values were decreased to 1.34, 1.85, 2.08, and 1.65 MPa for MGST, HBN, COMP, and STAC, respectively. Tablets made of MGST had the lowest tensile strength. When Fell and Newton (1970) equation was considered the cause of low crushing strength of tablets containing MGST explained the phenomenon. Even though the lubricant contents of tablets are a small percent, it is important to see to what extent they are extended on the granules, surface at the mixing procedure. MGST had apparently the largest extendibility and the lowest tensile strength among the lubricants, which eventually causes a decrease of tablet crushing strength with an increase of the concentration. The results complied with Shibata et al. (2002).

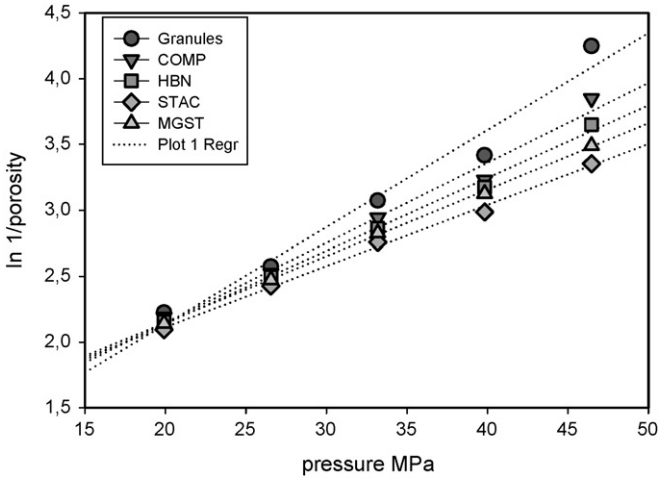


Fig. 7. Pressure *vs.* ln (1/porosity) graph of lubricated and unlubricated granules.

### 3.4. Compression behavior of tablets

The measuring of porosity changes as a function of the compression pressure is a method widely used in describing the compaction process of powder. The constants of the Heckel equation were determined by the linear regression analysis by using the least-squares method. Compaction characteristics Fig. 7 and Table 3 revealed that lubricated and unlubricated granule formulations were easily deformed under compression. In Table 4 constants and linear regression coefficients of granule formulations were given. For correct calculation of $r^2$ five pressure values were used (46.5, 39.8, 33.2, 26.5, and 19.9 MPa). All the $r^2$ values were found to be greater than $r^2 > 0.95$ and $r^2$ values gave the actual linearity of the plot. As it is seen in the Table 4 by the addition of 1% lubricant slopes of the Heckel equation were decreased. Granule, alone showed excellent binding and excellent plastic deformation. This is because of the added binder PVP K30. So, unlubricated granule had the biggest slope. However, including any lubricant plastic deformation starts to lean towards elastic deformation. Among the studied lubricants the most pronounced effect was observed with MGST at 1% concentration. The least pronounced effect was COMP and HBN at 1% lubricant concentration. Not having a negative effect on tablet porosity is the other positive effect of HBN.

Table 4
Constants and linear regression coefficients of Heckel equations (Eq. (2)) of lubricated and unlubricated granules

| Formulation | $A$ | $K$ | $r^2$ |
|---|---|---|---|
| Granule | 0.662 | 0.074 | 0.9719 |
| Granule-MGST | 1.137 | 0.050 | 0.9968 |
| Granule-HBN | 1.034 | 0.055 | 0.9959 |
| Granule-COMP | 0.933 | 0.061 | 0.9848 |
| Granule-STAC | 1.187 | 0.046 | 0.9969 |

In this study, evaluating different parameters, HBN was found to be as effective as MGST in reducing the LPEF when used at 0.5–1%. Moreover, when the other parameters were compared such as effect on disintegration time, tablet crushing strength, tablet tensile strength, and finally Heckel analysis HBN was found to be better than MGST. As a result our studies showed HBN can be used as a new lubricant in tabletting technology.

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