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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