EFFECTS OF LUBRICANTS ON BINARY DIRECT COMPRESSION MIXTURES

T. Uğurlu, M. Türkoğlu and M. D. Halaçoğlu

Marmara University, Faculty of Pharmacy, Pharmaceutical Technology Department
34668 Haydarpasa, Istanbul-Turkey

INTRODUCTION

The objective of this study was to investigate the effects of conventional lubricants including a new candidate lubricant on binary direct compression mixture. Magnesium stearate (MGST), stearic acid (STAC), glyceryl behenate (COMP) and hexagonal boron nitride (HBN) were tested. The binary mixtures were 1:1 combinations of spray dried lactose (FlowLac 100), dicalcium phosphate dihydrate (Emcompress), and modified starch (Starch 1500) with microcrystalline cellulose (Avicel PH 102). Tablets were manufactured on an instrumented single-station tablet press with and without lubricants. Studied lubricant concentrations were 0.5, 1, 2, and 4 %. In our previous studies (1, 2), we reported that magnesium stearate (MGST), and a newly introduced lubricant, hexagonal boron nitride (HBN) provided the smallest lower punch ejection forces (LPEF) during tableting for a wet granulation process. Whereas, stearic acid (STAC), and glyceryl behenate (COMP) resulted in much higher LPEF. A two way ANOVA design was used to evaluate these effects.

RESULTS AND DISCUSSION

Trials were made with four levels of (0.5, 1, 2, and 4 %) MGST, HBN, COMP, and STAC for all direct compression formulations.

![Figure 1: Effect of lubricant concentration on tablet crushing strength for DC1](FlowLac 100/Avicel PH 102 (1:1))

![Figure 2: Effect of lubricant concentration on tablet crushing strength for DC2](Emcompress/Avicel PH 102 (1:1))

![Figure 3: Effect of lubricant concentration on tablet crushing strength for DC3](Starch 1500/Avicel PH 102 (1:1))

MGST resulted in a biphasic curve, up to 1 % lubricant concentration a fast drop in crushing strength was observed for DC1, DC2, and DC3. From 1 % to 4 % lubricant concentration the curve was shallow (Fig. 1-2) except for DC3 where mechanical strength of tablets fell drastically (Fig. 3). It was well known from the literature that surface covering properties of lubricants are more drastic in the case of plastically deformed particles that unable to create new clean surfaces during compression (3). The other three lubricants, HBN, COMP, and STAC showed a shallow linear decline in tablet crushing strength vs lubricant concentration curves. The binary mixture Starch 1500 / Avicel PH 102 showed a steeper decline when compared to DC1 and DC2. This observation correlates well with less effective lubricant behaviour. However, in one of our previous reports (2) it was found that hexagonal boron nitride was as affective as MGST in term of lower punch ejection force. In the same study, COMP and STAC were much inferior in lowering the ejection forces (2). Based on the data obtained from Fig. 2-4, 0.5 % MGST addition as a lubricant with 3 minutes mixing time was not appropriate for a mechanically acceptable tablets regardless of binary combination in direct compression. Either less MGST will be used, or another effective lubricant such as HBN should be considered. It can be concluded that STAC or COMP will not be satisfactory lubricants at those concentrations.

For the statistical analysis, a two-way analysis of variance (2-way ANOVA) was separately performed for spray dried lactose-microcrystalline cellulose (DC 1), dicalcium phosphate dihydrate-microcrystalline cellulose (DC 2), and modified starch-microcrystalline cellulose (DC 3). The crushing strength was the dependent variable. Lubricant type and lubricant concentration were selected as the fixed factors. The General Linear Model / Univariate Analysis of Variance, main effects were evaluated. Bonferroni method was chosen for the Post Hoc Test. It was found that for all cases (DC 1, DC 2, and DC 3) there was a significant difference among the lubricants (p<0.0001).

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REFERENCES