Investigation of Abuse Deterrent Properties of Sintered Polyethylene Oxide and Hypromellose Placebo Tablets

Heather Boyce[1], Dan Smith[2], Steve Byrn[2], Bhawana Saluja[3], Wen Qu[3], Vadim J. Gurvich[4], Stephen W. Hoag[1]
University of Maryland School of Pharmacy[1]
Purdue University[2]
U.S. Food and Drug Administration[3]
NIPTE[4]

Background & Objectives

Abuse deterrent formulations (ADF's) have become a priority for both innovator and generic pharmaceutical companies as the abuse of prescription narcotics continues to rise[1-2]. It is important to understand how the physical barriers in currently marketed ADF products use polymer excipients to create increased tablet strength.

Specifically, Polyethylene oxide (PEO) is a common material used in ADFs [3]. PEO acts as a physical barrier to prevent tablet grinding, cutting, and breaking by increasing tablet strength. PEO also helps retard release from manipulated powders upon contact with water by forming gel. HPMC is also an excipient listed in the formulations of marketed ADF product. HPMC is a common filler agent in pharmaceutical dosage forms use to control the release of an active drug.

Sintering is a technique used in powder metallurgy to increase the strength of powders and alter their properties. It is therefore, interesting to examine how sintering can affect the breaking strength of a pharmaceutical tablet.

The objectives of this study were:

1. Determine key manufacturing properties that affect tablet strength
2. Identify key material properties that affect tablet strength

Methods

Table 1 outlines the 5 variables and their ranges selected for this experiment. Varying the combinations in Table 1 produced 5 blends (F1 to F5) resulting in 30 different types of tablets. 100% MCC tablets were used as a control.

Each blend was hand mixed for 2 minutes. The blend was placed in a Patterson Kelly V-Blender and blended at low rpm for 10min. 0.5 wt/wt% of MgSt was added and blended for 2 more minutes. The blend was transferred to a Manesty Betapress. Target tablet weight was 250 mg. Tablets were produced using two different forces. 20 Tablets from each formula were then sintered at the designated conditions in Table 1.

The tablets were then evaluated (N = 10):

- Tablet Crushing Strength
- Mass
- Thickness

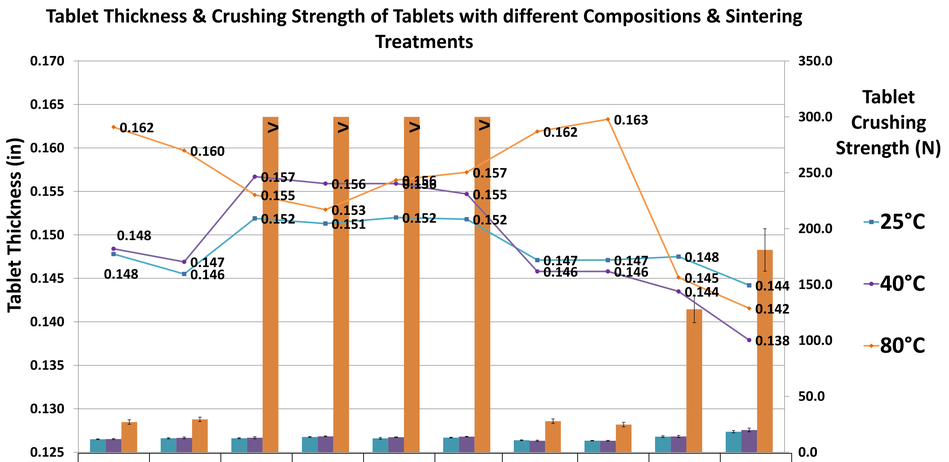
Table1. Selected variables and their ranges

PEO MW*10^6 (A)		PEO wt% (B)		HPMC wt% (C)		Compression Force (D)		Heat Treatment (E)		
-	+	-	+	-	+	-	+	-	+	++
2	5	10	30	10	30	10KN	15KN	None	12hr@ 50°C	12hr@ 80°C

Table 2. List of materials, grades, and their abbreviations

Excipient	Company	Abbreviation
Avicel PH 102, Microcrysalline Cellulose	FMC	MCC
Hydroxypropyl methylcellulose K4 Premium	Colorcon	HPMC
Polyox™ WSR Coagulant NF (5,000,000 MW)	DOW	PEO
Polyox™ WSR N60K NF (2,000,000 MW)	DOW	PEO

Results



F1	F1	F2	F2	F3	F3	F4	F4	F5	F5
2 MW	2MW	2 MW	2 MW	5 MW	5 MW	5 MW	5 MW	MCC	MCC
10% PEO	10 % PEO	30 % PEO	30 % PEO	30 % PEO	30 % PEO	10 % PEO	10 % PEO	MCC	MCC
30 % HPMC	30 % HPMC	10 % HPMC	10 % HPMC	10 % HPMC	10 % HPMC	30 % HPMC	30 % HPMC	MCC	MCC
10 KN	15 KN	10 KN	15 KN	10 KN	15 KN	10 KN	15 KN	10 KN	15 KN

Figure 1. Tablet crushing strength for each formulation and sintering treatment. F2 and F3 tablets sintered at 80° C had crushing strengths greater than what the instrument was able to record.

Tablet Strength was similar for all tablets not sintered (25° C) and when sintered at 40° C for 12 hrs. Tablet Strength increased significantly for all tablets sintered at 80° C. This indicates that sintering should occur above the melting point of PEO (MP = 65° C) for tablet strength to increase. Sintering of polymers typically occurs above the T_g of the polymer. PEO has a T_g = -70° C. Therefore, it is of interest to explain why sintering at 40° C did not alter table strength.

The molecular weight of PEO does not appear important for tablet strength within the 2 million to 5 million MW range of PEO (F1 vs F4 and F2 vs. F3, Figure 1).

Tablet compression force increased tablet strength of MCC (F5). Tablet compression force was not a significant factor for the other formulations.

The concentration of PEO used was significant. Tablets made with only 10% PEO/30% HPMC had tablet strength less significant than tablets made with 30% PEO/ 10% HPMC when sintered at 80° C. PEO concentration is important. 100% MCC tablets also exhibited a 10 fold increase in tablet strength.

After sintering, tablet thickness increased for the 10% PEO/30% HPMC formulation whereas the thickness for the 30% PEO/ 10% HPMC tablets remained the same. This correlates with the tablet crushing strength data. Lower tablet % porosity increases tablet strength. We believe that PEO may be sintered through a plastic deformation mechanism densifying the tablet. Since HPMC has a T_g = 170 – 180° C, these data indicate a unique mechanism that may be involved in the sintering of the 30% HPMC tablets.

Conclusions

PEO provides added strength to a tablet when the tablet is comprised of 30 % PEO and is sintered above its melting of 65° C. The molecular weight of PEO did not affect the tablet strength. Tablets made with only 10 wt% PEO and 30 wt% HPMC produced tablet strength that was insignificant in comparison to tablets made with 30 wt% PEO. All three polymers contribute significant results, however, the design of this study makes it difficult to discern the interactions and synergies that exist between MCC, PEO, and HPMC.

References

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