31T0400 # Influence of key polymer attributes, manufacturing conditions and sintering on abuse deterrence of physical barrier type abuse deterrent formulations (ADF)


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## Purpose

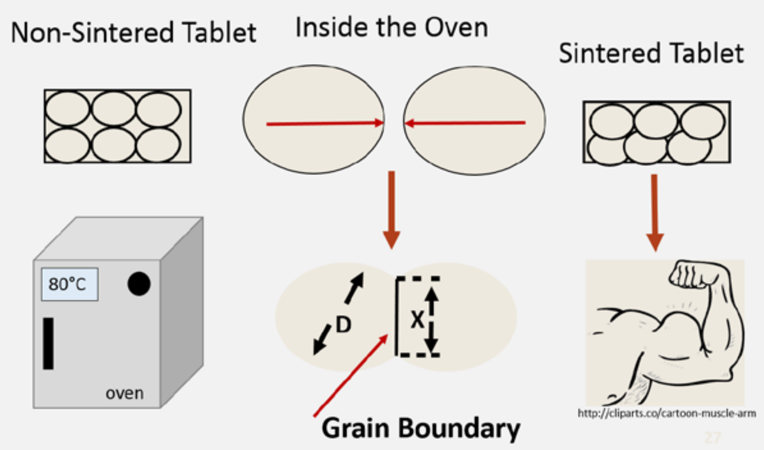
When sintering is used to treat tablet formulations containing polyethylene oxide (PEO), the polymer particles are able to form stronger bonds thereby increase tablet tensile strength. This increase in strength can make it more difficult for an abuser to break, chew, or grind opioid tablets. A mechanistic study was implemented to understand the key sintering factors that influence tensile strength.

## Methods

The ADF tablets were composed of PEO and inert filler dicalcium phosphate anhydrous. 10 mm flat faced tooling was used to compress the tablets on a Beta Manesty press.

Sintering Variables

- Tablet solid fraction (SF) [0.73, and 0.8] [0.77 used for SF PEO]
- PEO particle size [superfine & standard] standard size PEO taken directly from the container or SF PEO obtained from the sieve fraction of 150 to 250 µm was used.
- sintering time @ 80°C [0, 0.167, 0.5, 1, 3, 9 and 15 hr]
- Concentration of PEO [30, 50, 70 wt%]




Tablet Characterization Techniques

- SEM
- DSC (crystallinity)
- Pore diameter by Mercury porosimetry
- BET surface area
- Hardness Tester for tensile strength

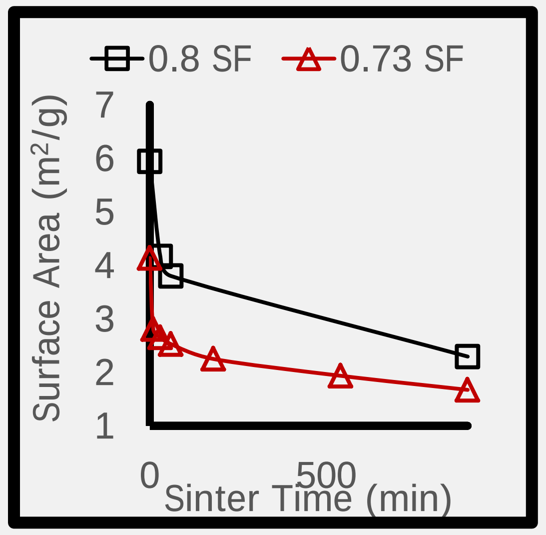
## Results

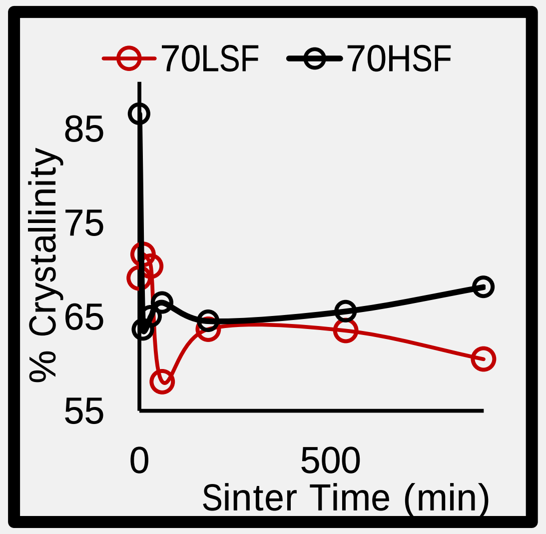
### Tablet Microstructure Characterization

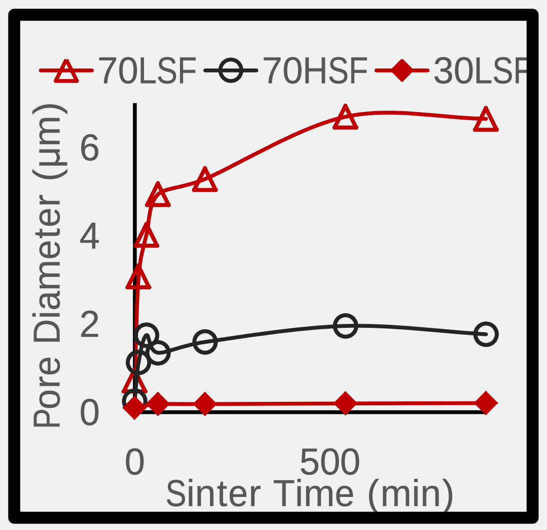
Significant tablet microstructural changes occur within the first 1 hr of sintering

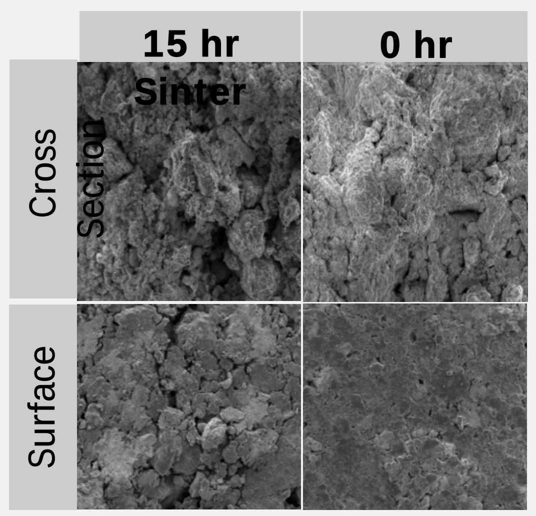
- Decrease in surface area
- Increase in pore diameter
- Decrease in PEO crystallinity

A rapid decrease in surface area within the first 10 minutes demonstrates the sintered particles' grain boundary grows rapidly (coarsening). Coarsening continues at later time points but it is not significant enough to impact microstructure or resulting strength. Pore diameter increases align with the observation that PEO rapidly coarsens under the study conditions. Mercury porosimetry shows that the degree of pore diameter coarsening is controlled by the initial solid fraction and the percentage of PEO in the dosage form. When all 30% PEO is present, there is no coarsening and therefore the tensile strength increases are minimal for the 30% PEO tablets. As the tablets are sintered the crystallinity of PEO decreases. The subsequent increase in PEO amorphicity increases the PEO ductility and therefore the overall strength of the dosage form.

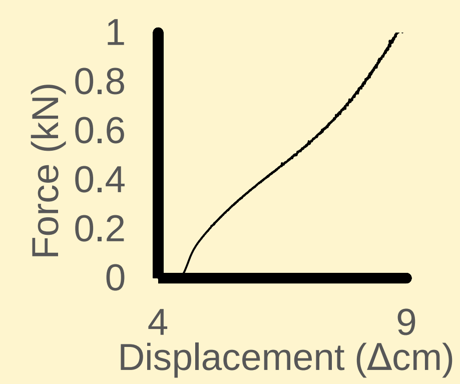


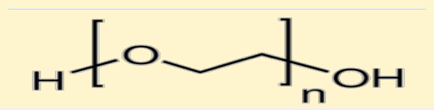




### Properties of PEO that lead to abuse deterrence




- Low Glass Transition: -70°C
- Linear backbone structure for highly ordered crystal structure
- Highly crystallinity >90% provides overall strength
- Amorphous components allow for toughness or exhibits ductile behavior



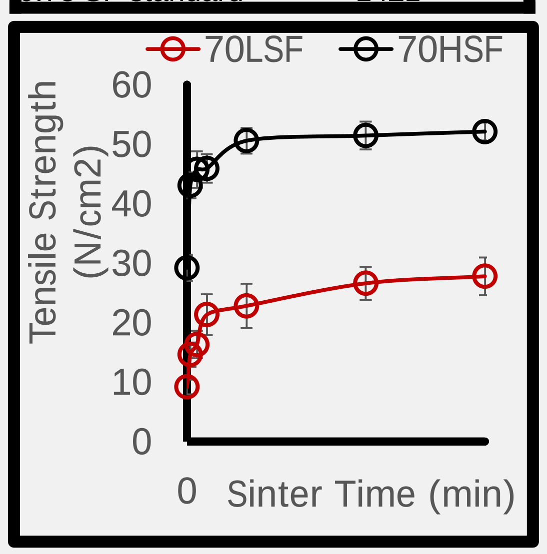

### Tensile Strength: Abuse Deterrent Response

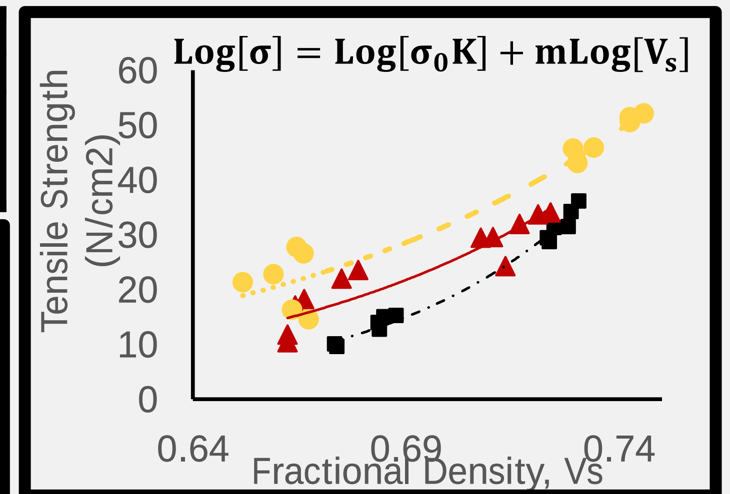
Tensile strength impacted by

- Fractional density at low PEO content (high m value)
- A smaller particle size distribution (SF PEO)
- High initial solid fraction

As the amount of PEO in the dosage form increases, the tensile strength becomes less dependent on solid fraction of the dosage form as indicated by high m values. The sintering time was found not to significantly increase the tensile strength after 1 hr of sintering. Significant tensile strength gains were only realized during first 1 hr of sintering in which significant tablet microstructure changes occurred. Finally, the super fine PEO demonstrated a huge increase in tensile strength in the non-sintered state. The sintered tablets made with superfine PEO were unable to be broken under compressive stress and 300 N.

| Tensile Strength ($N/cm^2$) Unsintered 70% PEO | |
|---|---|
| Super fine | 56 ±7 |
| 0.8 SF standard | 31±2 |
| 0.73 SF standard | 14±1 |




| Fit Parameters | 70% PEO | 50% PEO | 30% PEO |
|---|---|---|---|
| m | 8 | 10 | 15 |
| R2 | 0.84 | 0.79 | 0.99 |

## Conclusions

- When sintering PEO with dicalcium phosphate anhydrous at 80°C, the microstructural changes occur within 1 hour of sintering.
- The tensile strength increases only when the microstructure is changing; sintering between 1 to 15 hr does not yield any significant increases in tensile strength.
- The decrease in crystallinity results in more amorphous regions in the PEO lattice which could increase the ductility of the dosage form.
- A high initial solid fraction yields a more controlled sintering process.

## References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