Effect of Porosity on Weibull Statistics of Pharmaceutical Tablets

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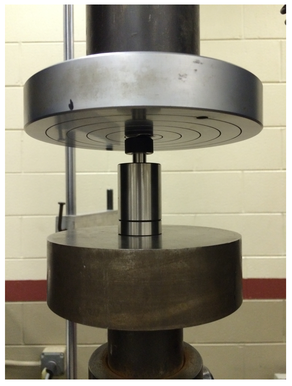
Abstract

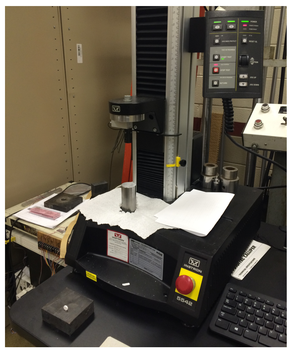
The pharmacy industry is responsible for development of new active materials with unknown properties. Despite the experimental and computational research in the pharmaceutical industry, the knowledge of creating reliable tablet strength is still unclear. In this respect, the aim of this research is to study effect of porosity on Weibull statistics, i.e., fracture statistics, of microcrystalline cellulose tablets. One of the biggest challenges in understanding Weibull statistics is the high number of samples (N>30) required to obtain significant statistics. Accordingly, in the present study, fracture statistics were obtained by testing fifty samples for each different porosity level. As a results, a total of 250 fracture tests were performed. The resulting data is presented in a Weibull plot to visualize variability in tablet strength (σ_f) and effect of porosity on σ_f. It was found that the Weibull modulus and fracture strength change not only with porosity, but also with the storage conditions. Weibull modulus was observed to decrease with increased porosity from ~17 % to 25 %.

Experimental Procedure

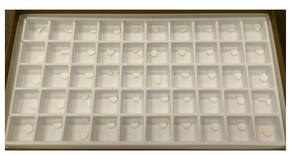


Load limited compaction

The type of the material used to create the tablets is called Avicel PH105, Microcrystalline Cellulose. It is a material based of wood and grass with a density of 1.46 g/cm^3 [1]. Using an MTS tensile test machine and a circular die set; the tablets were compressed to a fixed dimension of 2.5 millimeter thickness with a 10 millimeter diameter, to avoid size effects on fracture strength and its variability.



Tensile testing machine



One set of 50 samples

To create tablets of a set porosity (*P*), the equation:

$$P = 1 - \frac{\rho_{Tablet}}{\rho_{True}}$$

was used to solve for the density of the tablet. The particle density and the porosity are known since they are given. Converting the tablet density to mass with the given volume, the weight is derived to compress the tablets. The compaction force is then experimented with to compact the pill in the required dimensions.

Fracture strength of the tablets were obtained through diametral compression test using:

$$\sigma_f = \frac{2F}{\pi dt}$$

where *F* is the failure load, *d* is the diameter of the tablet, *t* is the tablet thickness [2]. Fracture data were fitted to two-parameter Weibull distribution:

$$P_f(\sigma) = 1 - \exp\left[-\left(\frac{\sigma}{\sigma_0}\right)^m\right]$$

where $P_f(\sigma)$ is the failure probability, σ_0 is the characteristic strength, and *m* is the Weibull modulus [3].

Results and discussion

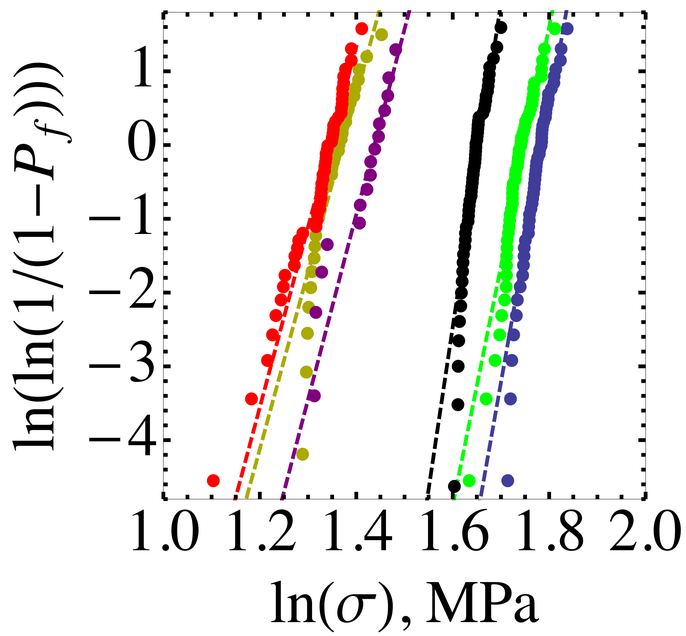


Figure 1. Weibull plot showing fracture strength of microcrystalline cellulose tablets of various porosity. Dashed lines represent Weibull fit to each fracture data with parameters m and σ_0.

m (90% CI)	σ_0, MPa	*P*, %	RH, %	N
37 (31-44)	5.97	16.8 ± 0.6	59	50
32 (28-38)	5.76	17.0 ± 1.2	47	50
44 (38-52)	5.24	18.4 ± 0.6	61	50
24 (17-35)	4.21	16.0 ± 0.8	54	16
24 (20-29)	3.94	17.6 ± 1.1	54	35
24 (20-29)	3.84	25.3 ± 0.5	53	50

CI is the confidence interval, P is the porosity with standard deviation, RH represents relative humidity during testing, and N is the number of specimens tested.

Environmental effects on fracture stochastics

Fracture strength of cellulose tablets are sensitive to humidity. This effect can be seen in Figure 2. The data sets other than the purple and yellow were kept in a open atmosphere box and fracture test was performed in 24 hours, after compaction.

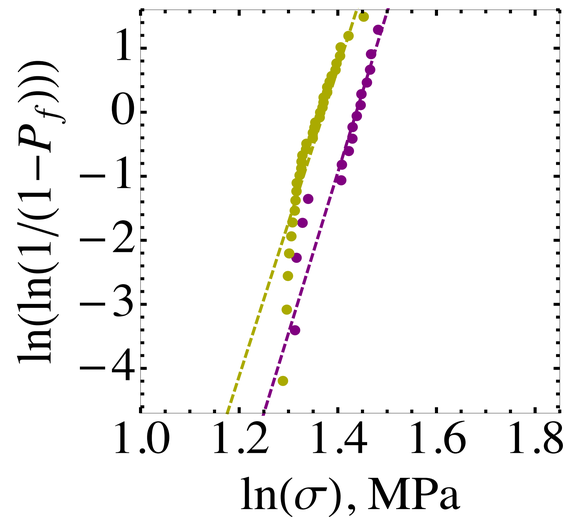


Figure 2. The effect of storage conditions on fracture strength of tablets that were produced in nominally identical way. Purple data represent results for tablets that were packaged in air-tight plastic bags, while the yellow data is for tablets that were in an open-atmosphere case. The fracture strength for the samples that were kept in the air-tight bags is greater due to the decreased humidity fluctuation.

Summary and conclusions

- Weibull modulus of tablets decreased for an increase in porosity from ~17 % to 25 %.
- Positive deviation from Weibull statistics was observed for specimens with P<20 %, tested in 24 hours after compaction [4].
- Fracture stochastics of microcrystalline cellulose tablets are sensitive to storage conditions.

Future work

- New set of fracture data will be generated for higher porosity levels, *P*>25 %.

Acknowledgement

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References

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[3] Weibull, W., (1951). Journal of Applied Mechanics, 13, 293-297.
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