Reduction of Sticking in Pharmaceutical Tablet Production

Nicholas Macke, William Morton, and Courtney Yonkers
Faculty Advisors: Professor Chelsea Davis, Ph.D.
Industrial Sponsors: Jon Hilden, Ph.D., Juan Carlos Rosario Borrero, Mark Polizi

The goal of this project was to reduce pharmaceutical tablet sticking during the tablet production process. With inspiration from biological surfaces[1], steel punch heads were etched to create surface roughness with Ra values of 2.3μm on both 9.5 and 12 minute etched surfaces. They were compared to an unetched punch head Ra of 0.9μm. Sticking was measured using UV-Vis spectroscopy of retained acetaminophen dissolved in ethanol. Etched surfaces exacerbated the problem with a 2,700 and 3,400 fold increase in sticking on the 9.5 and 12 minutes surfaces, respectively.

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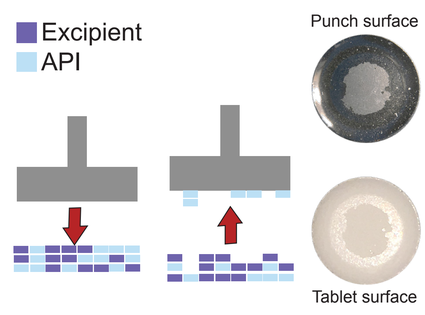
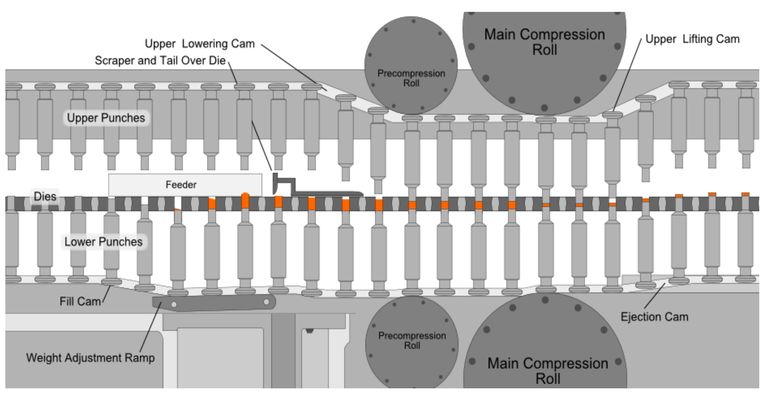
1.W. Barthlott, C. Neinhuis: Purity of the sacred lotus, or escape from contamination in biological surfaces, Planta, Vol 202, p.1-8, (1997)

Project Background

Compressed powder tablets are the most common form of delivery for active pharmaceutical ingredients (API). Production of these tablets often results in API sticking to the surface of the punch, eventually leading to the degradation of surface features on the tablet. By mimicking biological surfaces, secondary forces of attraction between the powder and punch can be minimized. Low amplitude surface features can be achieved using metal etchant techniques that result in superhydrophobic surfaces.

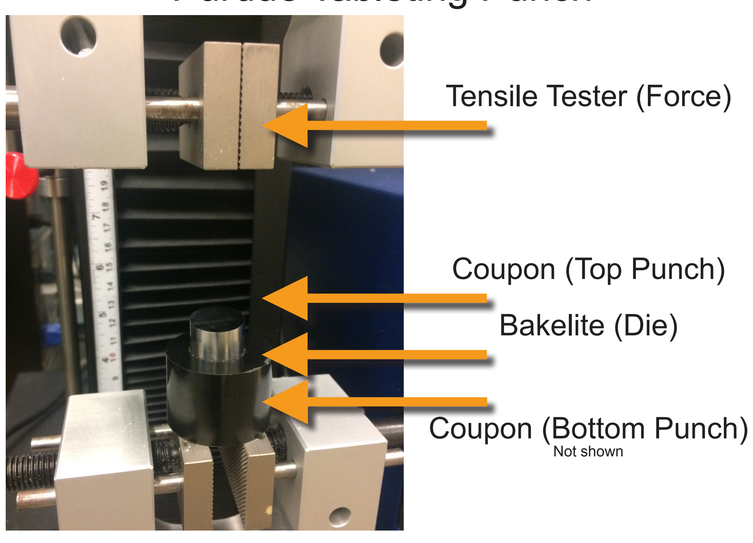




Punching Set-up

Using the coupons as punch heads, a die comprised of Bakelite, and a tensile tester for compressive force application, the Purdue Tableting Punch (PTP) was created. After each round of punching, the top punch (coupon) was agitated in ethanol to dissolve stuck APAP. Two pharmaceutical grade upper punches were etched and installed on a Flexi-tab research scale tableting machine at Eli Lilly's facilities, where they were compared to an unmodified punch. Characterization of the modified surfaces was achieved using a scanning laser microscope to obtain surface roughness (Ra).

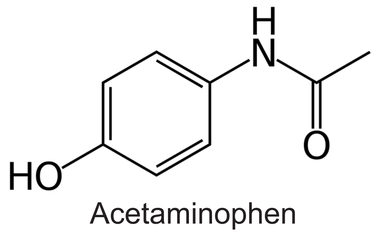
Purdue Tableting Punch



	Punch Force (MPa)	Punch Diameter (cm)	Tablets Punched	Ethanol Soak Time (min)
PTP	17.5	1.90	3	5
Flexitab	150	0.10	50	10

Sticking Characterization

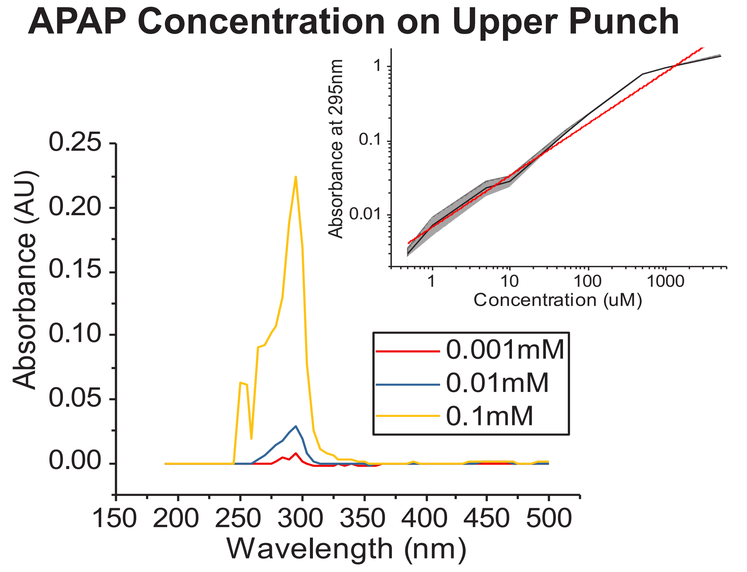
A powder formula was created using acetaminophen (APAP) as the API due to its high tendency for sticking. Surface modifications were performed on steel coupons via etching for various durations of exposure.



Acetaminophen

The ethanol-powder solution was run through UV-Vis Spectroscopy to measure the concentration of APAP in the solution. Energy dispersive x-ray spectroscopy (EDS) was performed on the surfaces of the coupons to ensure there were no contaminants present, and SEM was used to image the surfaces.

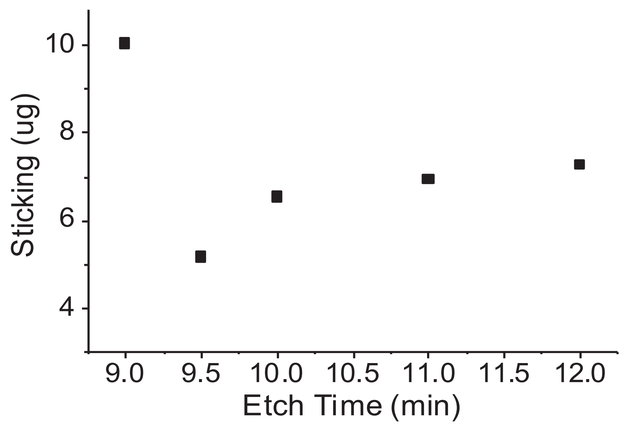
APAP Concentration on Upper Punch



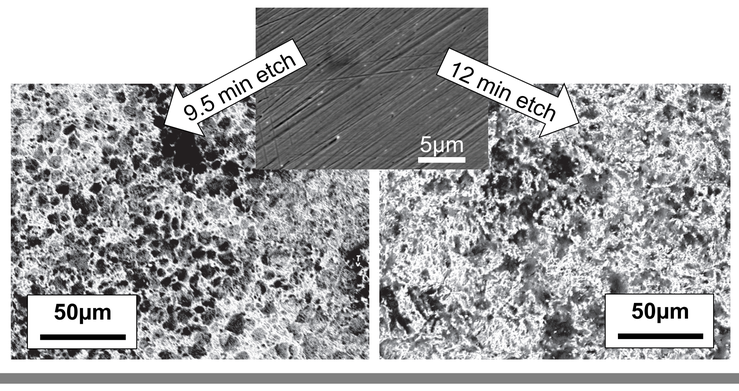
Results

Surface modification treatments were first tested on the PTP to determine which surfaces were most promising. The results of these preliminary tests can be seen below, with the 9.5 minute etched sample showing the least sticking.

Concentration of APAP on PTP



SEM supported the observation that longer etching times created smaller surface features, which are desirable to reduce sticking. These features can be seen in the SEM images below.

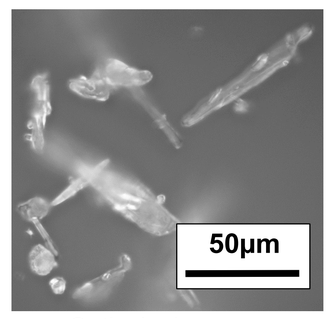


Discussion

The large distance between the surface features generated by etching, and inconsistent structures, allow for APAP to easily wedge itself into the surface, resulting in a large amount of immediate sticking.

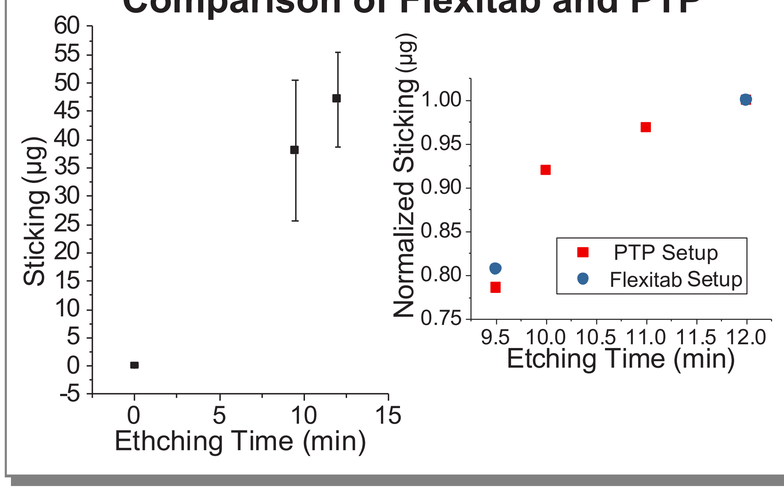
Etching Time (min)	SEM Feature Size (μm)	Roughness, R_a (μm)	Sticking (μg)
0	<1	0.91	0.0
9.5	~20	2.33	37.6
12	~10	2.35	47.0

The normalized sticking of the PTP and Eli Lilly tablet punches were very similar. This shows that the **PTP is an effective tool for predicting whether a surface modification will be successful when applied to a pharmaceutical punch.**



Optical microscopy image of APAP, which is about 5-10μm wide

Comparison of Flexitab and PTP



Conclusion and Future Work

Etching created uncontrolled and highly varied surface features that resulted in increased adhesive and cohesive forces. Therefore, smaller and more consistent surface features are required to accurately support our hypothesis. In the future this will be tested by creating a negative epoxy mold of a wrinkled polystyrene (PS) film through the experimental approach illustrated here.