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A Better Measure.

TABLET ROUGHNESS INSPECTION USING 3D PROFILOMETRY

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INTRO:

A tablet is a combination of active and inactive substances, in the form of a powder, which is pressed and compacted into a solid. The compressed tablet is the most popular dosage type used today. The inactive substances in a tablet, known as excipients, are used as carriers for the active ingredients of medication. Approximately two-thirds of all prescriptions are distributed as solid dosage forms. Approximately one-third of all prescriptions are compressed tablets.

In many instances, the active substance is not easily administered and absorbed by the human body. In these cases, the active substance can be mixed with or dissolved into an excipient. In order to create convenient and accurate dosages, excipients are also sometimes utilized to bulk up formulations containing very potent active ingredients. Also, excipients are added to tablets to ensure that the active substance remains "active" and stable for an adequately long period of time, such that the shelf-life of the product allows it to be competitive against other products.

EXCEDRIN

GENERIC EXCEDRIN

Types of excipients include: binders that hold the ingredients in a tablet together; glidants that are used to promote powder flow by reducing interparticle friction and cohesion; lubricants that prevent ingredients from clumping together and sticking to the tablet punches which ensures that tablet formation and ejection can occur with low friction between the solid tablet and the die wall; disintegrants that expand and dissolve when wet to cause the tablet to break apart in the digestive tract which releases the active ingredients for absorption; colors (pigments) that improve the appearance of a tablet and allow easy identification of medications; and sweeteners and flavors that are added to disguise unpleasant-tasting active ingredients and make them more palatable.

Coatings may also be applied to mask the taste of ingredients in a tablet and make the tablet easier to swallow by being less rough. Coatings also protect the tablet ingredients from moisture in the air, which causes the tablet to deteriorate. When a coating is applied, the tablet is more resistant to environmental conditions, which extends the shelf-life of the medication. Another reason a coating is applied is to control the location where the drug is released and to provide a continuous and controlled distribution of the drug. Lastly, a coating enhances the appearance of the tablet and preserves the chemical and physical integrity of the medication (drug).

ADVIL

GENERIC ADVIL

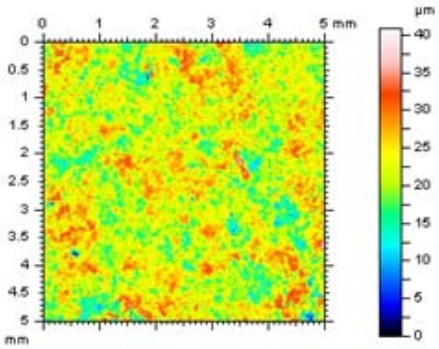
Tablet coatings need to follow the fine contours of embossed logos or characters on tablets, need to be stable and sturdy enough to survive handling of the tablet, and must not cause the tablets to stick to each other during the coating process. Current tablet coatings are polysaccharide and polymer-based, including pigments and plasticizers also. Film coating and sugar coating are the most common types of tablet coatings. Compared to sugar coating, film coating is less bulky, more durable, and less time-consuming to prepare and apply. However, film coatings have more difficulty hiding tablet appearance than sugar coatings.

In this application, the ST400 is used to measure and compare surface roughness values of different types of tablets. Excedrin, Advil, and generic forms of Excedrin and Advil, distributed by SUPERVALU Inc., are the tablets measured in this application. Comparisons can be made between generic and name brand tablet surface roughness, between coated and uncoated tablet surface roughness, and also among the same type of tablet to check the variations in surface roughness, mainly through the standard deviation.
(*The tablets used in this application note are commercially available).*

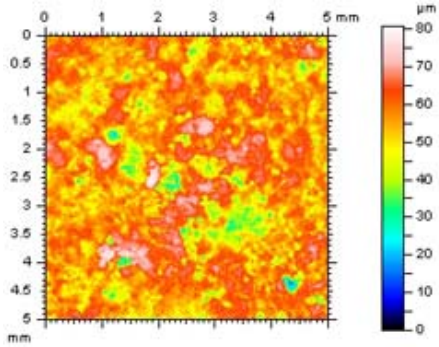
The two Excedrin batches measured in this study have been manufactured approximately one year apart. By measuring these two batches, changes in the manufacturing processes may be able to be detected. Excedrin Batch 1 was manufactured about 1 year before Excedrin Batch 2. The two generic Excedrin batches measured are tablets that came from the same bottle.

Hence, roughness changes over a period of time, one year, and the consistency of surface roughness of tablets manufactured at the same time, from the same bottle, can be observed.

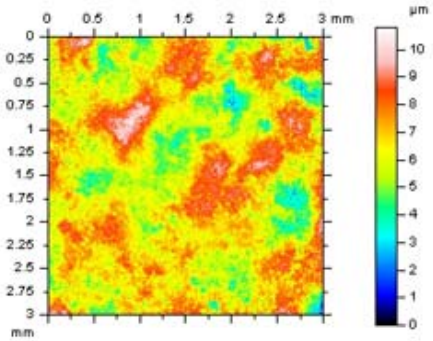
EXCEDRIN



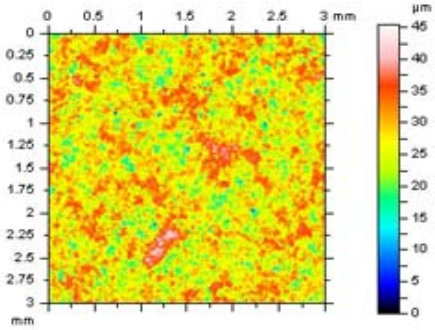
GENERIC EXCEDRIN



ADVIL



GENERIC ADVIL



TEST RESULTS:

TABLET ROUGHNESS VALUES

Excedrin	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
First Batch - 1	-1.334	11.03	3.949	37.52	49.69	87.21	2.843
First Batch - 2	-0.2306	5.082	4.192	34.45	39.22	73.66	3.244
First Batch - 3	-0.2708	4.204	3.705	23.2	26.39	49.6	2.871
First Batch - 4	-0.1274	4.239	4.585	31.14	29.83	60.97	3.557
First Batch - 5	-0.3594	4.692	4.687	33.44	49.83	83.27	3.61
Second Batch - 1	-0.1701	3.175	4.108	18.4	22.45	40.85	3.272
Second Batch - 2	-0.04555	3.284	3.489	18.27	24.76	43.03	2.759
Second Batch - 3	-0.4872	4.429	4.02	21.31	30.42	51.73	3.11
Second Batch - 4	-0.2514	3.572	3.623	14.73	26.24	40.97	2.863
Second Batch - 5	-0.07916	3.499	3.947	26.41	32.86	59.27	3.124

Generic Excedrin	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
First Batch - 1	-0.5951	4.845	5.288	33.3	41.77	75.06	4.081
First Batch - 2	-0.1334	5.109	5.554	33.24	64.26	97.5	4.26
First Batch - 3	0.481	13.92	8.276	44.93	108.4	153.3	5.383
First Batch - 4	-0.2954	3.58	6.359	29.42	41.77	71.2	4.971
First Batch - 5	-0.7841	6.278	5.862	38.02	48.92	86.94	4.238
Second Batch - 1	-0.5864	4.167	7.385	24.3	56.46	80.76	5.661
Second Batch - 2	-0.8875	6.002	5.448	28.35	52.25	80.61	4.15
Second Batch - 3	0.2855	4.871	7.024	38.53	35.79	74.32	5.346
Second Batch - 4	-0.3504	5.468	5.1	23.69	54.14	77.83	3.897
Second Batch - 5	-0.1001	4.423	6.754	33.03	46.97	80	5.218

Advil	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
1	-0.1322	3.072	1.285	4.23	6.57	10.8	1.02
2	0.03025	3.012	1.166	4.618	5.388	10.01	0.9318
3	0.03974	3.172	1.24	4.825	6.605	11.43	0.9799
4	-0.1616	3.185	1.219	5.375	6.099	11.47	0.9622
5	0.002918	2.775	1.189	4.269	4.824	9.093	0.9553

Generic Advil	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
1	-0.3934	3.47	4.574	17.71	27.73	45.44	3.607
2	-0.1652	2.88	4.733	17.96	21.83	39.79	3.799
3	0.5495	5.133	4.554	26.44	18.83	45.28	3.483
4	-0.2934	2.956	3.981	12.78	20.41	33.19	3.19
5	-0.1529	3.674	3.773	19.55	38.18	57.73	2.999

STATISTICAL RESULTS

Excedrin	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
Minimum (Batch 1)	-1.334	4.204	3.705	23.2	26.39	49.6	2.843
Minimum (Batch 2)	-0.4872	3.175	3.489	14.73	22.45	40.85	2.759
Maximum (Batch 1)	-0.1274	11.03	4.687	37.52	49.83	87.21	3.61
Maximum (Batch 2)	-0.04555	4.429	4.108	26.41	32.86	59.27	3.272
Mean (Batch 1)	-0.4644	5.849	4.224	31.95	38.99	70.94	3.225
Mean (Batch 2)	-0.2067	3.592	3.837	19.82	27.35	47.17	3.026
Mean (Combined)	-0.3356	4.721	4.031	25.89	33.17	59.06	3.125
Standard Deviation (Batch 1)	0.4411	2.61	0.3717	4.831	9.744	13.99	0.3256
Standard Deviation (Batch 2)	0.1576	0.4424	0.2391	3.898	3.788	7.249	0.1871
Standard Deviation (Combined)	0.3554	2.186	0.3674	7.485	9.41	16.29	0.2836

Generic Excedrin	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
Minimum (Batch 1)	-0.7841	3.58	5.288	29.42	41.77	71.2	4.081
Minimum (Batch 2)	-0.8875	4.167	5.1	23.69	35.79	74.32	3.897
Maximum (Batch 1)	0.481	13.92	8.276	44.93	108.4	153.3	5.383
Maximum (Batch 2)	0.2855	6.002	7.385	38.53	56.46	80.76	5.661
Mean (Batch 1)	-0.2654	6.746	6.268	35.78	61.02	96.8	4.587
Mean (Batch 2)	-0.3278	4.986	6.342	29.58	49.12	78.7	4.854
Mean (Combined)	-0.2966	5.866	6.305	32.68	55.07	87.75	4.721
Standard Deviation (Batch 1)	0.4366	3.688	1.065	5.325	25.07	29.73	0.5032
Standard Deviation (Batch 2)	0.4022	0.6731	0.9016	5.587	7.365	2.43	0.6982
Standard Deviation (Combined)	0.4209	2.793	0.9876	6.277	19.41	22.95	0.6231

Advil	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
Minimum	-0.1616	2.775	1.166	4.23	4.824	9.093	0.9318
Maximum	0.03974	3.185	1.285	5.375	6.605	11.47	1.02
Mean	-0.04418	3.043	1.22	4.663	5.897	10.56	0.9698
Standard Deviation	0.08525	0.1486	0.04124	0.419	0.6936	0.9052	0.02944

Generic Advil	Ssk	Sku	Sq (µm)	Sp (µm)	Sv (µm)	Sz (µm)	Sa (µm)
Minimum	-0.3934	2.88	3.773	12.78	18.83	33.19	2.999
Maximum	0.5495	5.133	4.733	26.44	38.18	57.73	3.799
Mean	-0.09108	3.623	4.323	18.89	25.4	44.29	3.416
Standard Deviation	0.3323	0.8128	0.3752	4.405	7.065	8.08	0.2873

TEST DISCUSSION:

From the roughness results, it can be observed that, in both cases, the mean average roughness (Sa) value for the name brand tablets were significantly less than the generic (comparable) forms of the same pill. Due to this, a conclusion can be made that there is definitely a disparity between the formula or formulation, or both, of the name brand and generic tablets. The name brand Advil was the smoothest and most consistent (in terms of surface roughness variations) of all the tablets featured in this examination.

There is a considerable difference in the standard deviation between Excedrin Batch 1 and Excedrin Batch 2. Since the average roughness values in Excedrin Batch 2 are more precise than the values in Batch 1, resulting in the standard deviation for Batch 2 being lower than Batch 1, it can be noted that there were some manufacturing changes in a period of one year.

The results seen in the standard deviation values of the generic Excedrin Batch 1 and 2 show that even though the tablets were manufactured at the same time and found in the same bottle, they had more inconsistency than any other type of tablet measured in this study. In fact, the generic Excedrin had a combined standard deviation value that was more than double the standard deviation of any other tablet in this trial. However, the mean average surface roughness falls in line with the expectation that the generic, uncoated tablet would be the most rough of all the kinds of tablets in this assessment.

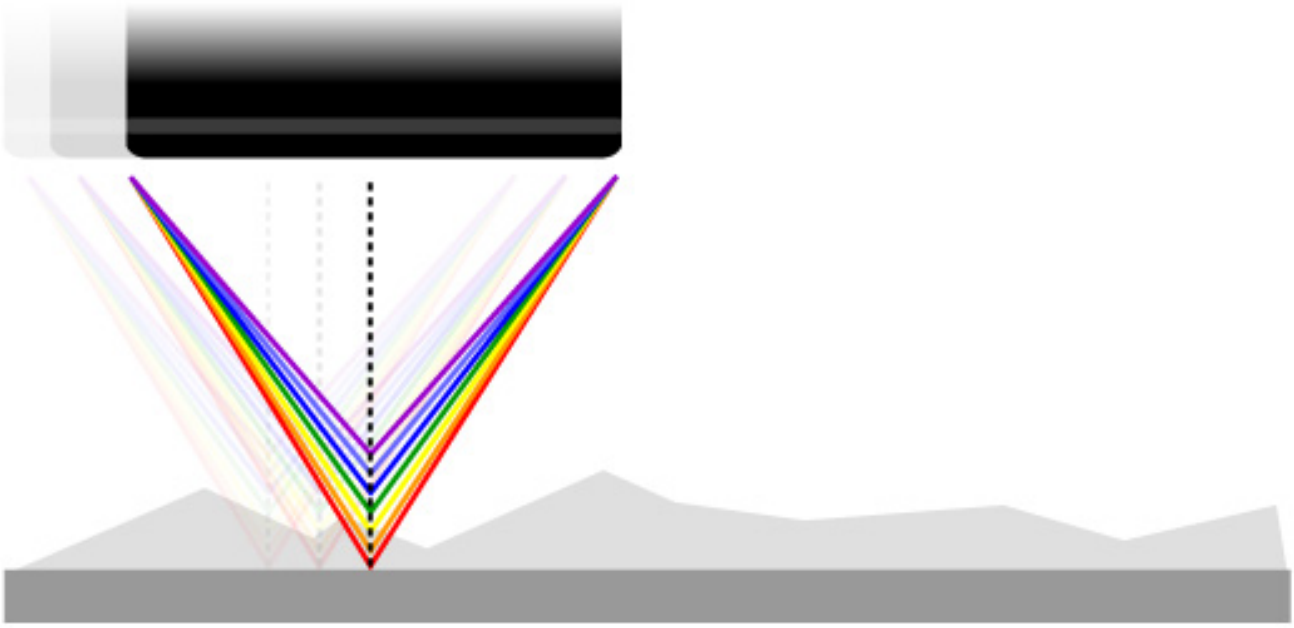
Lastly, the mean average roughness of the generic, coated Advil and name brand Excedrin disproves the assumption that coated tablets are always smoother (and easier to swallow) than uncoated tablets.

CONCLUSION:

The Nanovea ST400 and PS50 can be used to measure the surface of tablets (pills), from which surface roughness values can be calculated. Comparing roughness values of tablets is an extremely useful quality control tool to check and regulate the manufacturing processes. Due to the measurement technique of the ST400 and PS50, no stitching of images is required to measure a sizable area of a tablet and tablets with a dull coating, or no coating at all, can be measured without dropping data points. Lastly, creating and running a Macro measurement in the Nanovea 3D Software is a quick and very efficient method in which to measure a large quantity of samples. To learn more: Nanovea Profilometers

MEASUREMENT PRINCIPLE:

The Chromatic Confocal technique uses a white light source, where light passes through an objective lens with a high degree of chromatic aberration. The refractive index of the objective lens will vary in relation to the wavelength of the light. In effect, each separate wavelength of the incident white light will re-focus at a different distance from the lens (different height). When the measured sample is within the range of possible heights, a single monochromatic point will be focalized to form the image. Due to the confocal configuration of the system, only the focused wavelength will pass through the spatial filter with high efficiency, thus causing all other wavelengths to be out of focus. The spectral analysis is done using a diffraction grating. This technique deviates each wavelength at a different position, intercepting a line of CCD, which in turn indicates the position of the maximum intensity and allows direct correspondence to the Z height position.



Unlike the errors caused by probe contact or the manipulative Interferometry technique, Chromatic Confocal technology measures height directly from the detection of the wavelength that hits the surface of the sample in focus. It is a direct measurement with no mathematical software manipulation. This provides unmatched accuracy on the surface measured because a data point is either measured accurately without software interpretation or not at all. The software completes the unmeasured point but the user is fully aware of it and can have confidence that there are no hidden artifacts created by software guessing.

Nanovea optical pens have zero influence from sample reflectivity or absorption. Variations require no sample preparation and have advanced ability to measure high surface angles. Capable of large Z measurement ranges. Measure any material: transparent or opaque, specular or diffusive, polished or rough. Measurement includes: Profile Dimension, Roughness Finish Texture, Shape Form Topography, Flatness Warpage Planarity, Volume Area, Step-Height Depth Thickness and many others.

DEFINITION OF HEIGHT PARAMETERS

	Height Parameter	Definition
Sa	Arithmetical Mean Height	Mean surface roughness. $Sa = \frac{1}{A}\iint_A \lvert z(x,y)\rvert dxdy$
Sq	Root Mean Square Height	Standard deviation of the height distribution, or RMS surface roughness. $Sq = \sqrt{\frac{1}{A}\iint_A z^2(x,y)dxdy}$ Computes the standard deviation for the amplitudes of the surface (RMS).
Sp	Maximum Peak Height	Height between the highest peak and the mean plane.
Sv	Maximum Pit Height	Depth between the mean plane and the deepest valley.
Sz	Maximum Height	Height between the highest peak and the deepest valley.
Ssk	Skewness	Skewness of the height distribution. $Ssk = \frac{1}{Sq^3}\left[\frac{1}{A}\iint_A z^3(x,y)dxdy\right]$ Skewness qualifies the symmetry of the height distribution. A negative Ssk indicates that the surface is composed of mainly one plateau and deep and fine valleys. In this case, the distribution is sloping to the top. A positive Ssk indicates a surface with a lot of peaks on a plane. Therefore, the distribution is sloping to the bottom. Due to the large exponent used, this parameter is very sensitive to the sampling and noise of the measurement.
Sku	Kurtosis	Kurtosis of the height distribution. $Sku = \frac{1}{Sq^4}\left[\frac{1}{A}\iint_A z^4(x,y)dxdy\right]$ Kurtosis qualifies the flatness of the height distribution. Due to the large exponent used, this parameter is very sensitive to the sampling and noise of the measurement.
Spar	Projected Area	Projected surface area.
Sdar	Developed Area	Developed surface area.