PARTICLE CHARACTERIZATION OF OINTMENTS AND CREAMS USING IMAGE ANALYSIS

Ointments and creams used in the pharmaceutical and cosmetics industry may contain solid particles and/or emulsion droplets. Analyzing these particles in the final product is currently performed by manual microscopy or automated image analysis. Automated image analysis has the benefits of quickly measuring thousands of particles and reporting both particle size and shape distribution results. This study utilizes the PSA300 automated image analysis system to quantify the size and shape of various ointments and creams.

Introduction

Topical medication is applied to body surfaces such as the skin or mucous membranes. There are a wide variety of topical medication classes including ointment, cream, solution (powder dissolved in liquid), lotion (thicker, but similar to solution), gel (semisolid emulsion), foam (air as continuous phase), transdermal patch, powder (talc), solid (deodorant), sponge (some contraceptives), tape (cordran tape), and vapor (decongestants).

An ointment is a viscous semisolid preparation used topically on a variety of body surfaces including the skin and the mucous membranes of the eye (an *eye ointment*), vagina, anus, and nose. An ointment may or may not be medicated. The ointment base can be water, hydrocarbon, emulsion, or wax depending on the use of the product. The medication is dispersed in the base and later becomes divided after drug penetration into the living cells of the skin. Methods for preparing ointments include trituration where the insoluble drug is evenly distributed by grinding with a small amount of base followed by dilution with gradually increasing amounts of base, and fusion where the ingredients are melted together in descending order of their melting points and stirred to ensure homogeneity.

A cream is a topical preparation usually for application to the skin that is a semisolid emulsion (mixtures of oil and water) which may also incorporate a solid active ingredient. Creams can be oil-in-water composed of small oil droplets in a continuous water phase or water in oil composed of small water droplets in a continuous oil phase. Oil-in-water creams are more comfortable and cosmetically appealing since they are less greasy and can be easily washed away using water. Water-in-oil creams are more difficult to handle but hydrophobic drugs will be more readily released with this formulation, and are better moisturizers since they provide an oily barrier reducing water loss at the outermost skin layer. Many creams can be considered pharmaceutical products as even cosmetic creams are based on techniques developed by pharmacy and even un-medicated creams are used for a variety of skin conditions (dermatoses).

Experimental

A variety of over the counter (OTC) ointments and creams were purchased at a local pharmacy store. The samples used for this study include:

- Cortisone cream (1% hydrocortisone)
- Antibiotic ointment (emulsion)
- Cancer sore ointment (suspension)
- Exfoliating scrub

The samples were measured on the PSA300 image analyzer. All samples were analyzed by squeezing a small amount of ointment/cream onto the surface of a standard microscope slide and then using a flat razor to spread a thin, even coat across the surface of the slide. This approach appeared to work better than placing a slide cover over the sample and did not break fragile particles, as was observed when inspecting samples before and after a slide cover was applied. The sample was observed manually to determine the optimum magnification for the measurement. The 50x objective was chosen for the ointment and cream samples while the 25x objective was chosen for the exfoliant sample. Next a routine was created that optimized settings such as thresholding and edge definition for each sample. A pattern was created to analyze the portion of the slide containing the best sample dispersion/preparation. The PSA300 then automatically scanned the slide pattern, collected the images and processed the data using the chosen routine. The particle size distribution (volume based), roundness, aspect ratio, and compactness (1) were calculated and reported.

The advanced features of the PSA300 software were indispensable to collect and process the sample images, especially when air bubbles were present but not desired in the calculated results.

Figure 1: The PSA300 Static Image Analyzer

Unique software features (2) in the routines used for this study included multi-layer grab, contrast threshold, bridge removal, and closing.

Results

Table 1 below shows the results for the cortisone cream sample as described by the chosen size and shape descriptors. Note: PSD = spherical volume particle size distribution reported in µm, Round = Roundness, AR = Aspect Ratio, Comp = Compactness. All shape descriptor values are reported on a count basis. Figure 2 shows an image of the sample on the slide.

	PSD	Round	AR	Comp
d10	84.4	0.5	1.2	0.8
d50	127	0.7	1.3	0.9
d90	161.1	0.8	1.7	0.9

Table 1: Cortisone cream results

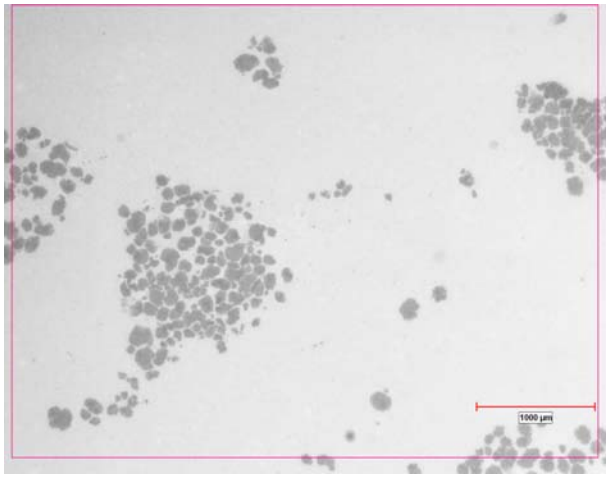

Figure 2: Cortisone cream image

Comments: The solid particles in the cortisone cream originally broke when lacing a slide cover on top of the sample. The method of spreading the sample with a razor did not fracture the particles.

Table 2 and Figure 3 below show the results for the emulsion ointment sample as described by the chosen size and shape descriptors.

	PSD	Round	AR	Comp
d10	18.8	0.8	1.1	0.9
d50	38	0.9	1.1	0.9
d90	61.1	0.9	1.2	1

Table 2: Emulsion ointment results

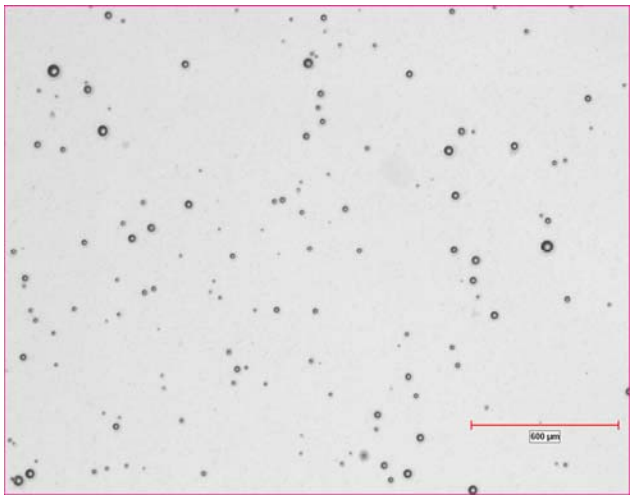

Figure 3: Emulsion ointment image

Comments: The emulsion droplets required careful threshold setting but otherwise this was an easy sample to analyze.

Table 3 and Figure 4 below show the results for the suspension (benzalkonium chloride) ointment as described by the chosen size and shape descriptors.

	PSD	Round	AR	Comp
d10	13.4	0.3	1.3	0.6
d50	42.5	0.5	1.6	0.8
d90	94.1	0.7	2.4	1

Table 3: Suspension ointment results

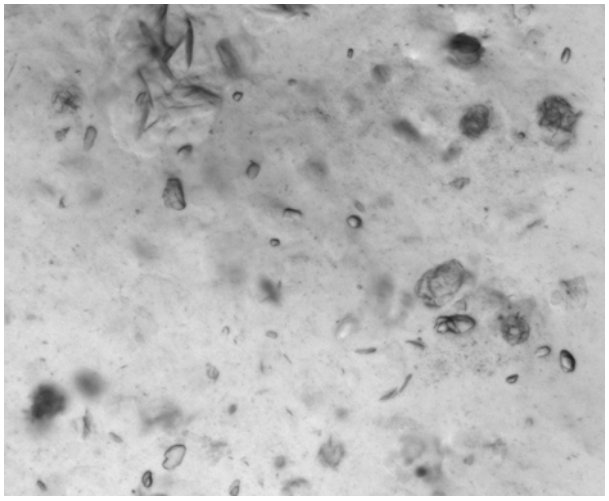

Figure 4: Suspension ointment image

Comments: This sample contained higher aspect ratio particles and required careful bridge separation to separate touching particles.

Table 4 and Figure 5 below show the results for the exfoliant sample as described by the chosen size and shape descriptors.

	PSD	Round	AR	Comp
d10	340.5	0.5	1	0.7
d50	475.6	0.7	1.2	0.9
d90	634.7	0.9	1.7	1

Table 4: Exfoliant results

Figure 5: Exfoliant image

Comments: The exfoliant sample was added in order to include another difficult sample in the study. This sample contained three particle species: large round beads, irregularly shaped particles, and air bubbles. The bubbles were removed from the results based on the level of transmitted light. The large beads and irregular particles could easily be sorted based on shape characteristics.

Conclusions

The PSA300 proved capable of defining the size and shape of particles, emulsions, and air bubbles in ointments and creams. Sample preparation was fairly easy and measurement times were under 5 minutes per sample. Particle size and shape characterization by automatic image analysis can be a valuable tool for the pharmaceutical and cosmetics industry making ointments and creams.

References

1. TN150 Size and Shape Parameters Defined in the PSA300, available from www.horiba.com/us/particle
2. TN152 Unique PSA300 Software Features, available from www.horiba.com/us/particle

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