

## The Effect of Milling on the Surface Area of Zinc Oxide Suspensions used in the Preparation of Sunscreen Formulations

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First produced in the Bronze Age as a by-product of copper-ore smelting, zinc oxide (ZnO) was early used as a skin therapeutic for healing of wounds (as a component of calamine) and for treatment of eyesores; it is also an effective fungistat. Because of its unique optical, thermal, electronic and chemical properties, ZnO is utilized in an extremely broad and diverse range of industrial, medical, pharmaceutical, agricultural and cosmetic applications (1); as an example, pharmaceutical grade (USP) ZnO is widely used today in burn ointments, as a skin protectant and in baby diaper rash creams.

Ultraviolet radiation (UVR) is a well-documented health hazard; UVB (290 – 320nm) is a complete carcinogen and the consequence of exposure to it is skin cancer (2). However, until relatively recently, what has not been totally appreciated is the danger from increased UVA (320 – 400nm) exposure; 99% of the total terrestrial UVR is UVA and it contributes significantly to the pathogenic effects of UVB (3).

Unfortunately, the use of sunscreen formulations containing actives that attenuate only UVB radiation appear to increase the risk for melanoma (4,5) since sunburn, as a warning for excessive exposure, is blunted. Thus, it is imperative that sunscreen formulations also attenuate UVA. Microfine ZnO is an effective and safe sunscreen agent that provides broad-spectrum (290nm – 400nm) UV protection (6, 7). The microfine grade of ZnO is distinguished from the regular USP grade material in that it has a particle size (PS) <200nm. At this size, visible light scattering is minimized to the extent that the particles appear transparent in thin films (8), such as those created when a sunscreen product - typically formulated as a water-in-oil (W/O) emulsion for beach use and as an oil-in-water (O/W) emulsion for daily wear (9) - is rubbed on the skin, making these products aesthetically acceptable. In the US, sunscreen products are regulated as drugs by the FDA and the sun protection factor (SPF) of a product is determined from *in-vivo* measurements of minimal erythema damage; the sun product is applied, using a 20-person panel, at a mandated concentration of 2mg/cm<sup>2</sup> of skin (10). Hence, of equal import (to PS) is the ZnO particle surface area per gram of material applied, since this directly impacts the UVR attenuation efficiency and, thereby, the SPF value.

Microfine ZnO is sold commercially typically as high solids suspensions in a variety of non-aqueous vehicles including mineral oils, fatty esters (such as isopropyl myristate), capric/caprylic triglycerides and silicone fluids (11); these are then incorporated into the “oil phase” of the specific W/O or O/W emulsion system used to deliver the active to the skin. Depending on material properties, conditions of manufacture and storage, all powders contain aggregates and agglomerates (8). Dispersing any dry inorganic powder material in a non-aqueous vehicle is not trivial (12)

but correct processing to remove agglomerates is essential in the formulation of ZnO-based sunscreen products since their presence impacts both performance and aesthetics – indeed, the importance of the process of dispersion and its profound effect on the economics and quality of the subsequent product has long been recognized (13,14).

In practice, a batch “premix” is first prepared and this slurry is then transferred to a milling device. Milling may be brought about through four basic processes: impact, shear, extension and cavitation and a variety of machinery is available including ball- and bead-mills, attritors and high-speed dispersers (15). However, no matter which method is used it is necessary to monitor the milling process over time to avoid costly and wasteful “over-milling”.

Since surface area changes with  $1/d^2$ , such measurements are sensitive to the presence not only of fines but also of agglomerates. Measurement of the surface area is commonly determined using BET ( $N_2$ ) gas adsorption (16, 17) but this requires the material under test to be a dry powder. However, drying wet suspensions inevitably results in aggregates and agglomerates and, as a consequence, the subsequent surface area measured by gas adsorption will be seriously underestimated. For wet suspensions of particles, as in ZnO/oil dispersions, it is essential, then, that the surface area be measured directly.

### **The Acorn Area**

The Acorn Area is a new instrument, using a patented technique based on NMR relaxation, to determine the wetted surface area of suspensions of particulate materials such as microfine zinc oxide (18). The Acorn Area takes advantage of the fact that liquid that is bound to a particle surface has a much lower relaxation time than the free or bulk liquid. Thus a sample with a high surface area will have a lower total relaxation time than a low surface area sample because there should be more of the fluid bound to the surface. Unlike, the measurement of particle size by, for example dynamic light scattering, where the raw intensity data has to be de-convoluted by means of complex algorithms, here the relaxation time can be converted into the absolute surface area by means of a straightforward calculation. However, as in the BET gas adsorption method, there is a basic assumption of monolayer coverage of fluid onto the particle surface.

The most common method of surface area determination is nitrogen ( $N_2$ ) gas adsorption (16, 17). In this method  $N_2$  is adsorbed on a sample kept at liquid  $N_2$  temperature at a series of different pressures. It requires that the dry powder sample be degassed to drive off any adsorbed material (sample conditioning); this requires a source of liquid  $N_2$  to maintain the proper sample temperature; and this is also a critical experimental requirement (19).

It is possible to calculate the surface area from measurements of the particle size but it assumes spherical particles and a monodisperse size distribution, a condition clearly not met by ZnO materials (20). Any surface area calculated for such materials is,

at best, only a crude approximation; it is well-recognized that particle shape, surface irregularities and porosity will inevitably lead to estimated values significantly less than the true value (21).

In contrast, the Acorn AreaA measures suspensions directly and requires neither sample pretreatment nor temperature control. There are no assumptions about the sample particle size (distribution) or shape used in the determination of surface area; it is measured directly. Thus, it is, inherently, a much simpler measurement technique; and as little as 0.1mL of sample is needed.

The formula for calculating the surface area from the measured NMR relaxation time is:

$$R_{av} = \psi_p S L \rho_p (R_s - R_b) + R_b$$

where  $R_{av}$  is the average spin relaxation rate constant,  $\psi_p$  is the particle volume to liquid volume ratio,  $S$  is the total surface area per unit weight,  $L$  is the surface layer thickness of liquid,  $\rho_p$  is the bulk particle density,  $R_s$  is the relaxation rate constant for the bound solvent and  $R_b$  is the relaxation rate constant for the free or bulk solvent.

Using a standard reference material we can define a constant,

$$K_a = L \rho_p (R_s - R_b)$$

so that the equation (1) reduces to:

$$R_{av} = K_a S \psi_p + R_b$$

The surface area can then be calculated from:

$$S = (R_{sp} - R_b) / K_a \psi_p$$

where,  $R_{sp} = R_{av} / R_b - 1$

A more precise method is to use the slope of a plot  $R_{sp}$  as a function of different volume ratios,  $\psi_p$  (i.e. concentrations).

## Results of Surface Area Measurements

To demonstrate the applicability of the Acorn Area to the measurement of the surface area of ZnO, we used two series of high solids suspensions of a microfine grade of ZnO. In the first, the ZnO was initially simply dispersed at approximately 52%wt/wt in C<sub>12</sub>-C<sub>15</sub> alkyl benzoate (widely used as an emollient in cosmetic formulations for the skin such as sunscreens and facial moisturizers) under high shear (rotor/stator) mixing. In the second, a dispersing agent – polyhydroxystearic acid – was added at a concentration of 0.1% and the ZnO concentration increase to 60%wt/wt. Both pre-mixes were then further processed using a cavitation device run at different (increasing) processing pressures.

Each suspension was sampled three times from the final bulk batches (each an undiluted fresh aliquot), the surface area measured directly and the data averaged. The results, summarized in Table 1 (and Figures 1 and 2), demonstrate the effect of the milling process on surface area for both formulation compositions.

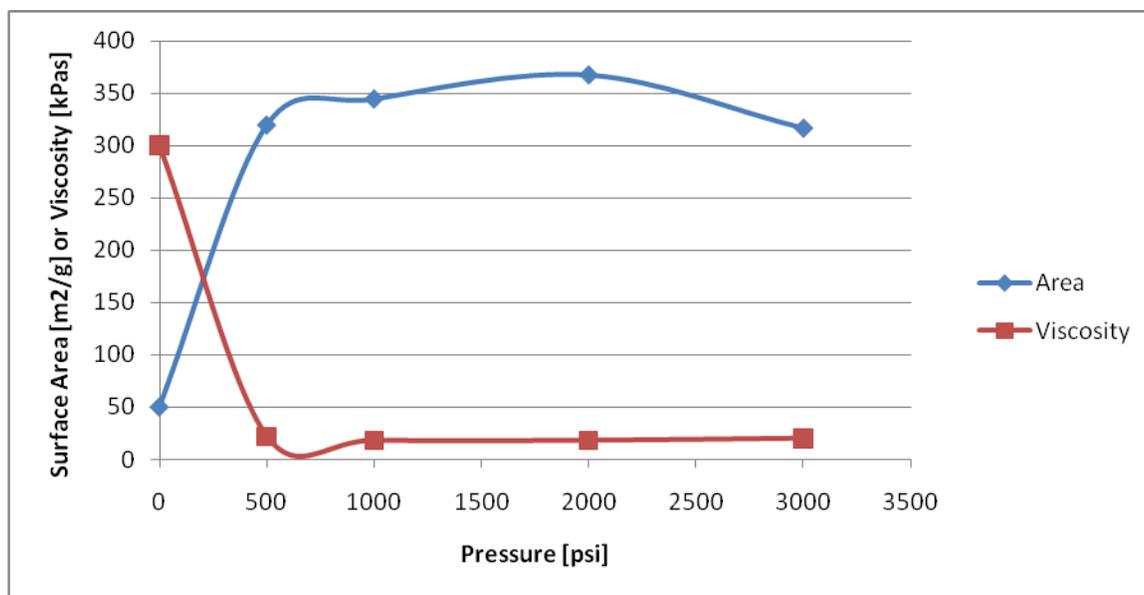


Figure 1: Surface Area and Viscosity as a Function of Mill Pressure No Dispersant

In the first series (Figure 1), it can be seen that, for this particular ZnO material, milling at pressures over 2000 psi is, clearly, counter-productive. Given the effect on performance features, together with the economic implication of over-milling, a direct measurement of the wetted surface area without dilution or other sample preparation is critical in production quality control (QC). This is now available for the first time with the Acorn Area. Since the measurements can be made in minutes, a milling process can be monitored virtually in real-time to obtain optimum conditions thus saving time and money.

The second series (Figure 2) also demonstrate the dramatic effect of the addition of a dispersing agent. With the use of only 0.1% PHSA, the solids loading can be significantly increased without any detrimental change in pre-mix viscosity but, importantly, the surface area increases from  $50\text{m}^2\text{g}^{-1}$  to  $180\text{m}^2\text{g}^{-1}$ ; these factors all provide economic advantages or a manufacturer. The data further suggests that the Acorn Area could be used to optimize the amount of dispersant used. For this series, optimum milling is achieved at around 1500 psi.

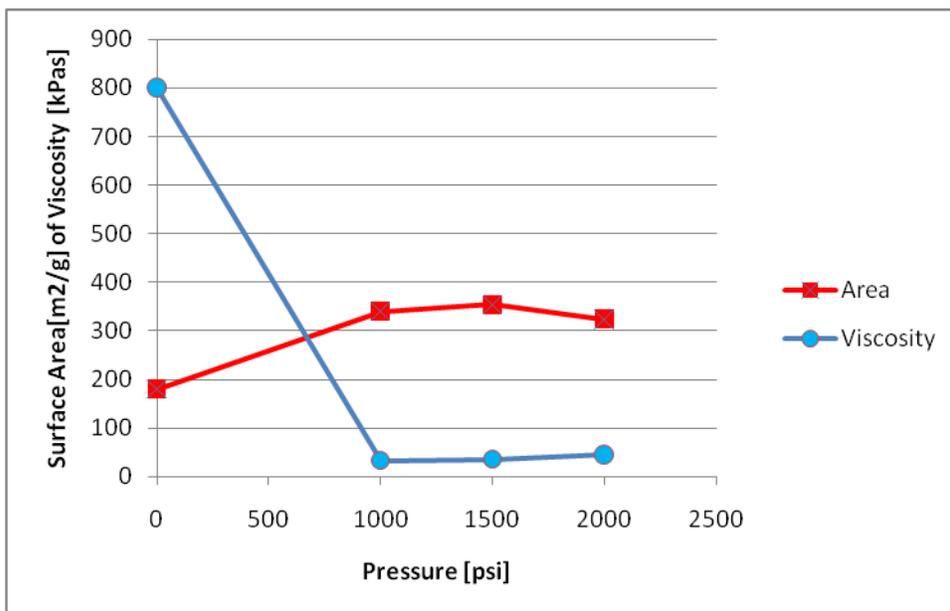


Figure 2 Surface Area and Viscosity as a Function of Mill Pressure With Dispersant

In Table 1 we also compare the surface area data with that from rheological measurements (on the same samples); rheological characteristics determine suspension functionality (22, 23). Although the flow behavior of real commercial suspensions is complex – the systems are visco-elastic (VE) - it is directly related to the particle size distribution (PSD) of the dispersed phase (24). Thus, milling should result in changes in VE profile and this is supported here by the low-shear-rate viscosity and yield value data for the two series of samples; milling initially decreases the dispersion viscosity. A lower viscosity means that the ZnO dispersions are easier to pour making them more “processable”, an advantage since these materials will subsequently be used in the preparation of emulsions.

Finally, the correlation of milling with surface area measurement is quite clear. Rheological measurements do not appear to be as sensitive. Further such instrumentation is, however, costly and requires a skilled operator and so, unlike the Acorn Area, does not conveniently lend itself to QC use.

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**TABLE 1**  
**Summary of Surface Area and Rheology of ZnO Dispersions**

SAMPLE	SURFACE AREA m <sup>2</sup> /g	VISCOSITY (kPa·s)	YIELD (Pa)
<b>(a)52% ZnO – no dispersant</b>			
0	50	300	20
500	320	22	8
1000	345	18	8
2000	368	18	8
3000	317	20	10
<b>(b)60% ZnO – 0.1%PHSA</b>			
0	180	800	0.2
1000	340	33	0.6
1500	354	36	1.5
2000	324	45	3