# Application Report

## Nano particles

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Force Tensiometer – K100

## Nanoparticle Surface Energy Determinations

Smaller Particles – Smaller Problems


### Abstract

A nano particle is a particle with at least one dimension in the range of 100 nm or less. Nanoparticles can be formed from a vast variety of materials, typically by rapidly diminishing the solubility of the material and condensing it into exceedingly small individual particles. Much research goes into specific nanoparticle formation methods, often employing such rapid condensation techniques as super critical fluid (SCF) expansion, micro-mixing, and the like. Much has already been gained in terms of the commercial application of nanoparticles, because of their extreme surface areas on a per mass basis. Nanoparticles (nano-dispersed colloids) are already at work in such everyday products as cosmetics, ink, stain resistant clothing, and even more durable tennis balls. In the electronics industry, nanoparticles made of semi-conducting material (so-called "quantum dots") bridge the gap between bulk materials and atomic structures in terms of the way they conduct current. In medicine, the uses are seemingly without end – from wound patch applications, to growth inhibitors for tumors, to enhanced drug delivery for inhalables and transdermals. In these, and most nanoparticle applications, the enhanced surface area of nanoparticles based on their smaller size is the key. With that comes the need for understanding what the exact nature of that surface is, in terms of its abilities to interact with (adhere to) other surfaces, as well as to be dispersed in the case of colloidal applications. In other words, the component surface energies of their surfaces need to be identified and understood.

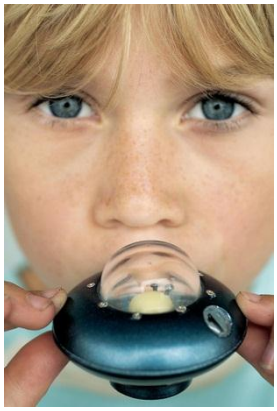
## Methods

For surface energy determinations on particles, one's choices are typically inverse gas chromotopgraphy (IGC) type vapor sorption techniques or the Washburn wicking technique. IGC-type techniques are inherently very difficult to interpret, time consuming, and saddled with the errors associated with first determining the exact surface area per gram of the material. Washburn techniques, for some powdered materials, can also be problematic if the particle size varies largely, the powder is difficult to pack reproducibly, or there is surface heterogeneity – as in mixed powder systems like drugs with excipient for pharmaceuticals (see KRÜSS Application Note AN302e).

IGC methods get no easier on nano particles versus larger particles, the same problems persist despite the larger surface area per gram. However, our experience is that the Wasburn method does get easier. Our lab has now looked at a dozen or more different types of nanoparticles for surface energy and found them to pack better than more macroscopic particles (which is not overly surprising based on their smaller sizes) and to have more reproducible packing factors (material constants) and contact angles.

## Experiment

In this offered example we compare three lots of porcine insulin which is being studied as a precursor to human insulin studies for inhalable insulin applications.

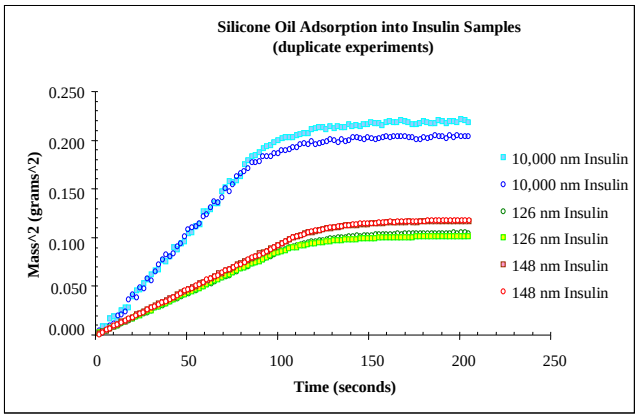


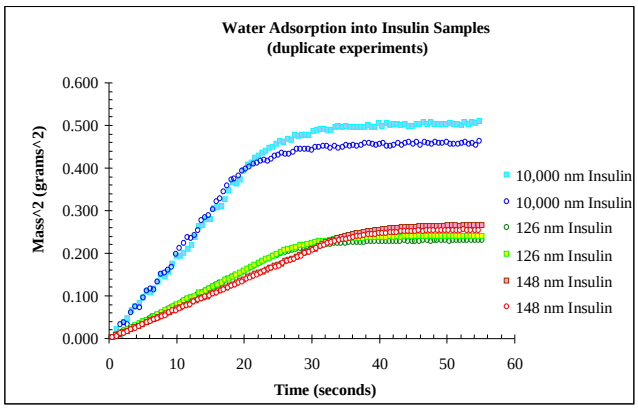
Inhalable insulin – relief for many diabetics
Photo : Eric Anthierens (Licence)

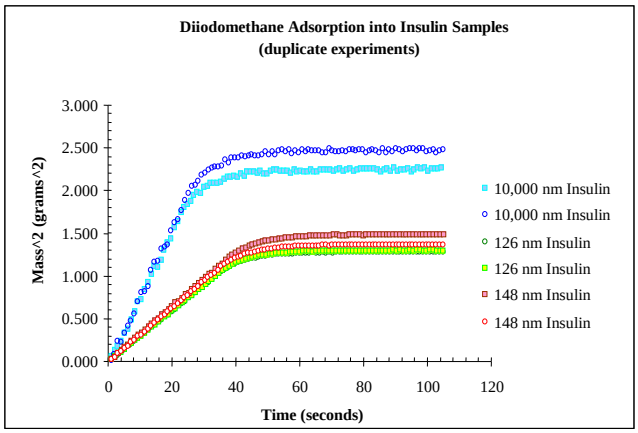
The nano particle lots are of interest, because they are believed to be more efficient as well as more compatible to atomization in the base dispersion (sol-vent/insulin/surfactant) which is aerosolized. Their surface energies, and most particularly their surface energy components, are important because they dictate the types of surfactants necessary to disperse the insulin in its base solution, and may also have an, as yet not completely understood, impact on adsorption to the inside of the lung. Using the Washburn method with the KRÜSS Force Tensiometer – K100, we studied:

1. Insulin Standard (10,000 nm particle size)
2. Insulin ethanol prepared (148 nm particle size)
3. Insulin SCF $CO_2$ prepared (126 nm particle size)

A low molecular weight, low surface tension, silicone oil is used as the material constant determination fluid and water and diiodmethane are used as the surface tension determination liquids, along with the Fowkes theory. We studied 0.5 gram samples of each material, per test. As can be clearly seen in the graphs below, a better reproducibility for the duplicate tests on the nanoparticle samples compared to the 10,000 nm sample was achieved.



Material constant and contact angle data from these three duplicate experiments were as follows:

| Insulin Type | Material Constant ($cm^5 \times 10^6$) | Water Contact Angle (degrees) | Diiodomethane Contact Angle (degrees) |
|---|---|---|---|
| 10,000 nm | 5.3816 | 57.4 | 43.2 |
| 10,000 nm | 5.4201 | 58.4 | 45.9 |
| 148 nm | 2.3210 | 65.0 | 48.2 |
| 148 nm | 2.3183 | 65.3 | 48.0 |
| 126 nm | 2.1393 | 58.4 | 47.0 |
| 126 nm | 2.1440 | 58.3 | 46.9 |

## Results

Larger measurement-to-measurement differences occurred between the material constants and contact angles for the 10,000 nm insulin (+1.0° for water and +2.7° for diiodomethane) compared to the 148 nm and 126 nm insulin samples (which showed no contact angle difference greater than 0.3 for both liquids). When surface energy values are calculated, this translates into about a 1.5 $mJ/m^2$ error bar on surface energy determination and about a 1.0% error bar on surface polarity determination for the large particle insulin – as opposed to a tight 0.2 $mJ/m^2$ and 0.4% error bars on the surface energy and surface polarity for the nanoparticle insulins.

Results will naturally vary, with type of nanoparticle tested. However, in our experience, unless the quantity of nanoparticles available is very little, the greater surface area is no reason to choose IGC methods for the characterization of nano particles. The increase in surface area may slightly improve the resolution of the required surface area. However, even at its best, the variability of surface area determinations is +/-3% to 5%. And, that's just for an input parameter – not counting the error associated with the vapor sorption measurement itself. Nanoparticles pack so well that Washburn analysis is far more reproducible than that, on virtually all particles, but most especially on nanoparticles.

The following surface energy results are calculated for the three insulin samples, based on the contact angle data listed above. One surface energy calculation is done from each contact angle set to highlight the error bars discussed above.

| Insulin Type | Overall Surface Energy ($mJ/m^2$) | Surface Polarity (%) |
|---|---|---|
| 10,000 nm | 50.75 | 25.19 |
| 10,000 nm | 49.38 | 26.03 |
| 148 nm | 45.02 | 21.65 |
| 148 nm | 44.93 | 21.25 |
| 126 nm | 49.05 | 26.75 |
| 126 nm | 49.14 | 26.77 |

You will note that the 10,000 nm insulin, which was the material used to form the other two samples by ethanol (148 nm) and super critical $CO_2$ techniques (126 nm) has about the same surface properties as the $CO_2$-formed nanoparticles. The ethanol formed particles have a lower surface energy and surface polarity – which was important information for our customer.

## Summary

The Washburn technique is very useful for the characterization of contact angles on nanoparticle materials which lead directly to surface energy data. Nanoparticles pose no significant problems for Washburn technique use, and in fact, at least in our experience, are better candidates for accurate contact angle work than are most powders with larger particles, as long as enough amounts (2 grams or greater typically, for the overall surface energy characterization) of the nanoparticles are available for testing. Studies into three insulin samples showed that the effect of the nano particle formation method on the surface energy could be clearly detected with the Washburn method.