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Keynote speech

Application and characterization of nanomaterials in consumer products

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Nanotechnology is science, engineering, and technology conducted at the nanoscale (1-100 nanometers). Nanoscience and nanotechnology are the study and application of extremely small things in diverse applications including chemistry, biology, physics, materials science, and engineering. Production and application of nanoparticles in consumer products is at an all-time high.

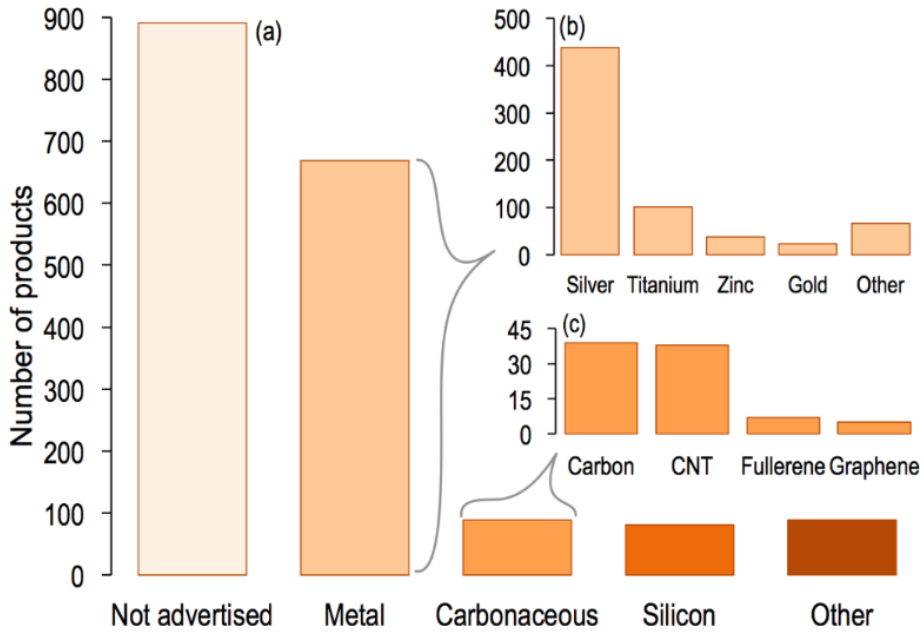

Figure 1: Composition of nanomaterials listed in the consumer product inventory (Beilstein J. Nanotechnol. 2015, 6, 1769–1780)

Direct detection and quantification of trace levels of nanoparticles within consumer products such as food, sunscreens, or dietary supplements, is an important challenge. Consumer products are often complicated mixtures that may contain inorganic nanoparticles composed of gold, silver, titanium dioxide or zinc oxide. It is important to understand the properties of nanoparticles that appear in consumer products. A variety of techniques are

used to describe metal content, elemental composition, oxidation state, size, size distribution, shape, and surface charge of nanomaterials. All of these often interrelated parameters can influence how nanomaterials interact with the consumer and the environment and may influence the behavior of the particle in a complex system.

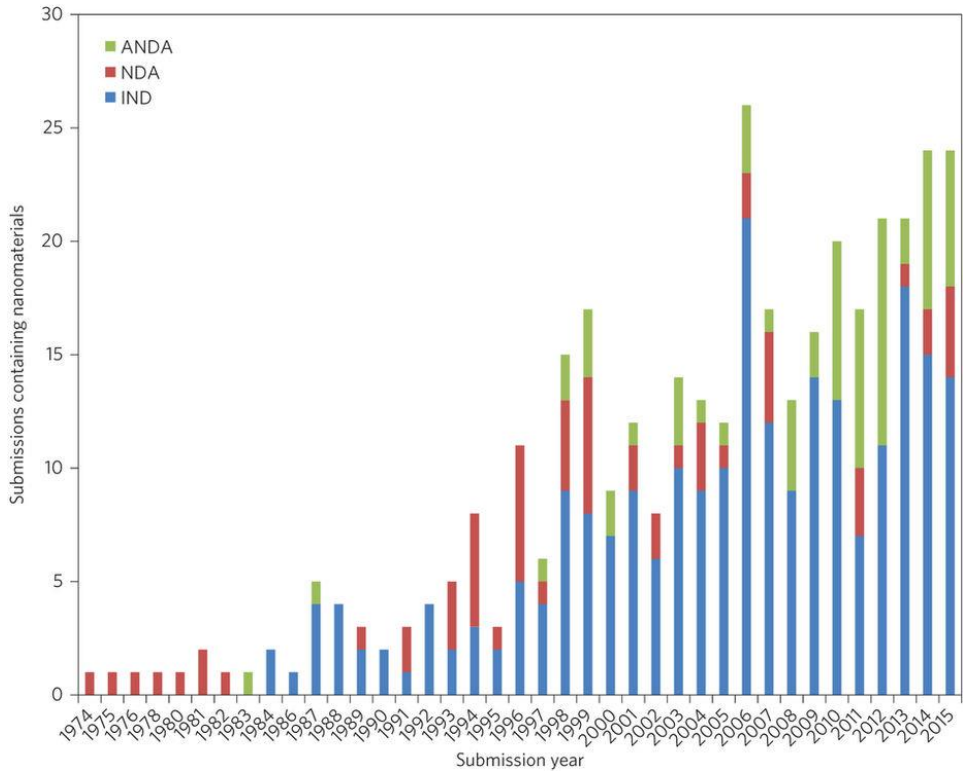

Figure 2: Number of nanomaterial product applications submitted to FDA by year (*Nature Nanotechnology* **12**, 523–529 (2017))

Nanomaterials are also used in drug formulations and/or targeted drug delivery systems. Their unique properties have led to an explosion of nanomaterial product applications submitted to the FDA (Figure 2). Liposomes are prime examples of organic nanomaterials currently used in approved drug formulations and dietary supplements. Liposomes are a closed compartment made up of phospholipid bilayer and an active pharmaceutical ingredient (API) which is either encapsulated inside the liposomes (Liposomal Doxorubicin) or trapped in the lipid bilayer (Liposomal Amphotericin B). Encapsulation of the API inside the liposome reduces the toxicity of the formulation related to the free API and increases

the circulation time of the formulation in the blood. Water insoluble APIs such as Amphotericin B, partition in the lipids bilayer of the liposomes provides the drug delivery mechanism. Encapsulated active ingredient content, lipid profile, size, and zeta potential are determined in the characterization of liposomal products.

This presentation will describe several developed methodologies for characterizing inorganic and organic nanoparticles using microscopy techniques, light scattering, size-based separation methods, elemental analysis, and mass spectrometry. Determination of the size and size distribution are most important parameters in the characterization of nanomaterials. Therefore, selected size based separation techniques for the characterization of nanomaterials will be presented in detail.

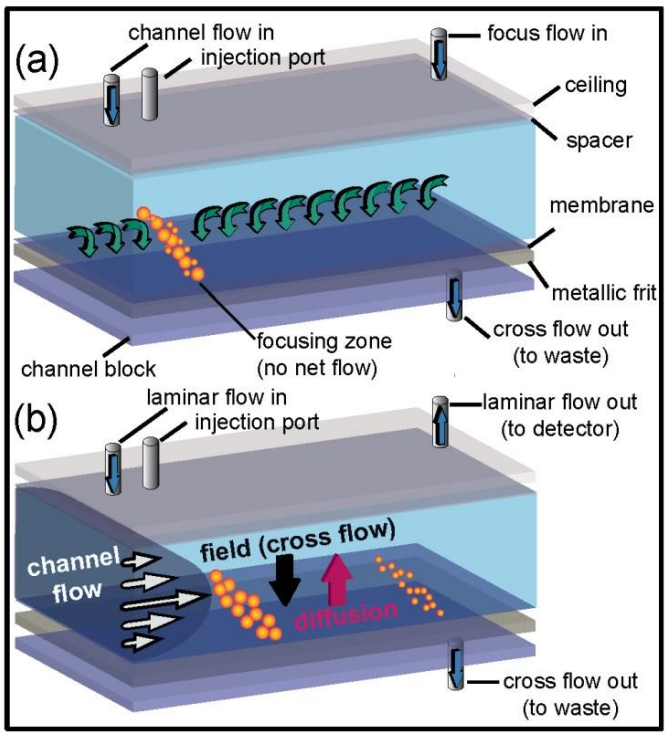

Figure 3: Schematic illustration of AF4 channel assembly showing the liquid flow profile during the (a) focusing and (b) separation steps

1. Asymmetrical flow - field flow fractionation (AF4)

AF4 is a diffusion based separation technique, which uses narrow ribbon shaped channel. One side of the channel is lined with porous membrane supported by metal frit. As indicated in Figure 3b, the liquid flow along the

channel (channel flow) creates a parabolic flow profile where center of the channel has a greater flow rate along the channel compared to flow rate at edge of the channel. As shown in Figure 3b. fraction of the liquid entering the channel passes along the channel and a fraction passes through the membrane providing a downward cross flow. The cross flow pushes nanoparticles towards the membrane and diffusion bring them back towards center of the channel. Smaller particles, having a higher diffusion coefficient, travel further away from membrane towards the center of the channel and move faster along the channel due to parabolic flow profile providing size based separation mechanism.

AF4 analysis consists of 2 steps, which are focusing and separation. In the focusing step, fluid is pumped into the channel from both ends simultaneously. All fluid entering the channel escapes as crossflow through the membrane and nanoparticles are concentrated as a narrow band, near the injection port where there is no net flow of fluid along the channel as schematically illustrated in Figure 3a. Focusing is an essential step to achieve good resolution in fractograms. In the separation step, analytes separate based on their size (diffusion coefficient) with particles eluting from smallest to largest.

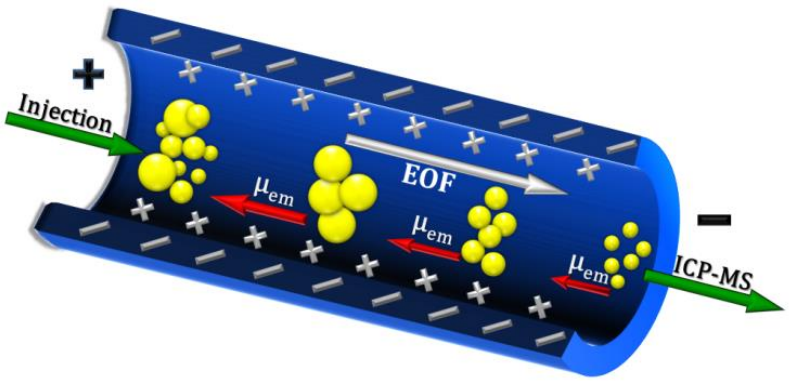

Figure 4: Illustration of the separation of a nanoparticle mixture using capillary electrophoresis

2. Capillary electrophoresis

Capillary electrophoresis uses narrow fused silica capillaries and an electric field to separate charged analytes according to charge and size. In normal mode of operation, the capillary's inner surface is negatively charged. Positively charged counter ions balance the charge of electrolytes within the

capillary and create a net positive free ion excess within the capillary. When a high voltage (0-30kV) is applied along the capillary, negative electrolytes migrate towards the anode and positive electrolytes migrate towards the cathode. Since there is an excess of free positively charged electrolytes, migration of cations creates a net fluid flow from the positive electrode to the negative electrode. This bulk flow of liquid based on the electric field is called electroosmotic flow (EOF). The EOF can be minimized by coating internal surface to make it neutral or direction of the flow can be changed by inverting surface charge of the inner wall of capillary. Unlike conventional pressure driven laminar flow profile (parabolic flow) electroosmotic flow generates a flat flow profile in narrow capillaries, which helps to minimize peak broadening in the separation.

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