Modern Methods of Particle Size Analysis

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CHAPTER

2

THE APPLICATION OF PARTICLE CHARACTERIZATION METHODS TO SUBMICRON DISPERSIONS AND EMULSIONS

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1. INTRODUCTION

Characterization of the size of component particles in industrial dispersions is often required for research purposes and is a routine and essential part of the overall quality control procedures invariably applied to the products. Characterization methods have been extensively reviewed (1–3), but if the average particle in a dispersed system is at or below the limit of discrimination by the light microscope (about 1 μm), many of the regular sizing methods become inappropriate. Submicron dispersed systems have become technically more important during the past decade in a number of industries, and methodology for sizing has shown a parallel development.

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The biological activity and effectiveness of pesticides and herbicides are critically affected by the size of the active component used for application. As a result, submicron systems have been developed for commercial use.* In pharmacy, the effect that particle size has on the biological activities of water-insoluble drugs has been well-recognized for many years (4). However, the reduction of solids to submicron-sized powders is expensive and counterproductive. Not only are electrostatic surface forces exposed, which results in the aggregation of the fine particles, but handling such systems also inevitably leads to an increased risk of dust explosions and cross-contamination problems in a factory environment. In addition, there is an increased risk to health when workers are exposed to the possible inhalation and absorption of often potent bioactive materials. In these situations, it is more advantageous to handle the bioactive materials as emulsions or as dispersions in solid–liquid systems. In these forms, manipulation and processing are facilitated.

In the medical field, fine (submicron) emulsions of vegetable oils are now routinely administered to patients as parenteral calorie sources. In these products, it seems likely that administration of sufficient numbers of emulsion droplets close to or greater than the dimensions of a blood capillary could produce undesirable side effects (5). Quality control procedures applied to those systems should ideally determine that the products do not contain appreciable numbers of particles larger than a micron. Intravenous emulsions also offer some promise as drug delivery systems, and the same is true for liposomes or phosphatide vesicles varying in size from 10 to 1000 nm (6). In both cases, it is likely that a critical performance factor is size (7).

Outside the biological and medical areas, the performance of pigment dispersions in terms of covering capacity and color development is also critically controlled by the size of the primary pigment particles and the number of primary particles forming aggregates (8). Although not emulsions in the strict sense of the term, polymer latex emulsions are widely employed as paints. Essential properties, such as covering capacity, penetration, film-forming ability, "brushability," and stability are all critically influenced by the mean size and spread of size around the mean. Frequently, polymer emulsions are in the submicron range and much of the recent progress in size characterization methodology can be directly attributed to developments in this particular industry.

* A list of addresses for manufacturers of commercially available instruments is given in the Appendix.

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2. THE MEANING OF THE TERM "SIZE" IN A SUBMICRON DISPERSION

Intuitively, the term "size" in a macroscopic system means the diameter of the average particle, and is often associated with some parameter that provides a description of the width of the size range from the smallest to the largest particle in the system. If the particles can be seen and measured, this concept provides little or no difficulty, and sizing methodology enables the appropriate parameters to be determined.

However, when dealing with submicroscopic or submicron systems, semantic problems arise, because situations occur where a hard and fast definition of the term "particle"—and, therefore, of "size"—becomes somewhat imprecise.

Submicroscopic particles are usually referred to as colloids. A colloid can be defined as a two-phase system with *discrete* particles of the disperse phase that are between 1 and 100 nm (10–1000 Å).

These limits are somewhat imprecise in themselves and are intended to describe particles that are smaller than the lowest level of discrimination by the light microscope, but are capable of detection by the Tyndall beam effect. For example, Faraday prepared colloidal gold solutions that appeared to be clear when placed directly between the observer and a light source. When viewed laterally, however, the light appeared as a yellow track in the solution, and this was interpreted as being due to light scattered from the dispersed gold particles at right angles to the incident beam.

The colloidal size range encompasses macromolecules as well as aggregates of smaller molecules. The surface forces around an aggregated colloidal particle are less per unit mass than the forces around the constituent molecules, if they were dispersed in a "true" solution. The fundamental properties of true and colloidal solutions are the same qualitatively, but differ quantitatively, because of the differences in particle size and structure. There is also a range of size in which particles between approximately 0.1 and 2–5 μm have properties between colloids and those of macroscopic dispersions or suspensions. The behavior of colloidal particles is influenced strongly by their environmental conditions. This provides a challenge when attempting to characterize the size of particulate systems with diameters anticipated to be below 5 μm, since properties of the systems can be readily affected by the conditions under which the analysis is carried out.

In addition, it is necessary to closely consider what is actually defined as the "size" of a colloidal particle, especially with particles below 50

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