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REVIEW ARTICLE

Measurement Techniques and Pharmaceutical Applications of Zeta Potential: A Review

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Abstract

This review article deals with measurement and applications of zeta potential. Zeta potential (ζ) is the potential difference between the dispersion medium and the stationary layer of fluid by which dispersed particle are surrounded. Stability of colloidal dispersions (e.g. multivitamin syrup) directly depends upon the zeta potential of system. All material acquire a charge spontaneously when come in the contact of polar medium by different charging mechanism viz. affinity differences of two phases, ionization of surface groups, differential ion adsorption from electrolyte solution, differential ion dissolution from a crystal lattice, surface anisotropy and isomorphous substitution. The zeta potential indicates the degree of repulsion between adjacent, similarly charged particles in dispersion. For molecules and particles that are small enough zeta potential will exhibit stability, i.e., the solution or dispersion will resist aggregation. There are four measurement methods for zeta potential viz. electrophoresis, electro osmosis, sediment potential and streaming potential. When the zeta potential is low, attraction exceeds repulsion and the dispersion will break and flocculate. In pharmaceutical field measurement of zeta potential is used as key to understand dispersion and aggregation processes and also used to determine the presence or absence of charged groups/moieties on the surface of materials. In this review, the significance of zeta potential including its method of measurement and commercial importance in various areas are discussed.

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INTRODUCTION

The zeta- potential is an important parameter that is related to the surface charge that possess by all material when dispersed in polar or non-polar medium. It is the potential difference between the dispersion medium and the layer of fluid surrounding the dispersed particle. In the layer of fluid surrounded the dispersed particles contain oppositely charged liquid ions. When the charged particles move through the liquid medium then the liquid layers surrounding the particles also move. It can help to maintain the more consistent product and also help in improving the product quality and performance. In addition zeta potential plays a very important role in flotation and flocculation process.[1]

Development of Electrical Properties in Aqueous Media

There are number of different charging mechanism by which particle acquires charge when dispersed in aqueous media:[2]

Affinity Differences of Two Phases for Electrons

This mechanism is involved in the development of contact potential difference (electromotive force) between two dissimilar materials if they are electrically connected and also have a significant role in corrosion and thermoelectric effect.

Ionization of Surface Groups

This mechanism is involved in the development of charges on the surfaces of all metal oxides and as well as on materials that contain carboxyl group and/or amino groups such as protein, polyelectrolyte, ionic polymer. The ionization and/or dissociation of these groups and the net molecular charges depend totally on the pH of the dispersion medium.

Differential Ion Adsorption from Electrolyte Solution

In this mechanism, unequal adsorption of oppositely charged ions on the materials surfaces and resultant materials surfaces becomes a total net either positive or negative. Many lyophobic material suspensions (polymer latexes and APIs) come under this category.

Differential Ion Dissolution from Crystal Lattice

Ionic solids, such as calcite ($CaCO_3$), hydroxyapatite [$Ca_5(PO_4)_3(OH)$] and barite ($BaSO_4$) can gain a surface charge by this mechanism due to unequal dissolution of the oppositely charged ions.

Surface Anisotropy

This mechanism is involved in the anisotropy of crystal lattices. Charge development occurs because of n and p defect in the crystal. Minerals oxides such as silica[3] show this effect.

Isomorphous Substitution

It is exhibited mainly by the clay materials such as monmorillonite and vermiculite. In this, the material acquires large negative charge because of the valancy difference between the Al^{3+} and the Si^{4+} ions in the alumino-silicate crystal structure. [4,5,6]

Development of Electrical Properties in Non-aqueous Media

In the solvents having moderate dielectric constants (greater than 10 and equivalent to water) some extent of ionization is possible and charging mechanism approximately similar to those occurs in polar medium. For example, low molecular weight alcohol, amines, aldehyde and ketones, ionic surfactants and some ionic salts. Particle dispersed in such a medium with very low dielectric constant value ≈ 2, electrostatic forces are important in stabilizing such systems. But the charging mechanism is not the same as in aqueous dispersions. It may be assumed that it occurs due to acid-base (or electron donor-acceptor) interactions between the particle surface and the dispersing agent.[7,8,9] Due to this acidic (Poly Vinyl Chloride) or basic (Poly Methylmethacrylate) polymers are effectively suspended in non-aqueous media.
The electrical charge and surface charge on the particle in non-aqueous media is very complex but technically is very important and its impact on pharmaceutical preparation is extensively reviewed by formulator.[10,11]

Electrical Double Layer

In contact with a polar medium such as water, the majority of particles show definite surface charges. The surface charges affect the arrangement of neighboring ions of polar medium. Ions of the opposite sign also called *counter ions* will be attracted to the particle surface and the ions of the equal sign also called *coions* will be repulsed from the surface. The resultant electrical double layer will be developed in such a manner that it neutralizes the particle surface charge. The electrical double layer can be regarded as consisting of two regions or layers: a region closest to the surface (the Stern layer) that is considered immobile (and it may include adsorbed ions) and an outer region (it may include diffused ions that are distributed according to the influence of electrical forces and random thermal motion).[12,14,15,16] Extent of double layer is influenced by the solution condition such as pH, ionic strength, temperature and pressure.[17] It has a very useful parameter in monitoring the electro kinetic behaviour of suspensions.[18]

The electric potential decreases linearly from ψ_0 (the actual *thermodynamic* surface potential) to the Stern potential, ψ_d and then it decays exponentially to zero in the diffuse layer. It can be explained by simple mathematics model in equation 1:[19]

$$\psi = \psi_d \exp [- \varkappa x] \qquad (1)$$

Where, ψ = Thermodynamic surface potential
ψ_d = Stern potential
x = Distance from the particle surface
$\varkappa$ = Debye-Hückel parameter

The Debye-Hückel parameter can be calculated by the formula:

$$\varkappa = [2e^2 N_A c z^2/\varepsilon\varepsilon_0 k_b T]^{1/2} \qquad (2)$$

Where, e = Proton charge
N_A = Avogadro's constant
C = Concentration of electrolyte
z = Valency of electrolyte
ε = Dielectric constant
ε_0 = Permittivity of free space
k_b = Boltzmann constant

Methods for Measurement of Zeta Potential

There are many materials available in the market that supplied by the various manufacturer.[1] These are well characterized particles suspended in the systems having electrophoretic mobility. For example: Goethite, it is an official reference material.[20]

Electrophoresis

It is extensively used due to its simplicity and giving quick results. Electrophoresis has been revealed when a fine dispersion of some dielectric matter in the electrolytic solution is exposed to the effect of an electrical field. Dispersed particle acquires a charge according to dispersion medium; resultant electric double layer is formed. If a liquid phase is prevented to flow in one direction, and the charged particle is allowed to keep in motion in electrical field, they will travel towards cathode or anode according to their charge.

Electro-osmosis

Electro-osmosis is the measurement of the flow of a liquid phase through a porous membrane in the presence of an electrical field with constant temperature. Speed of electro osmotic flow depends on strength of electric field applied on the charged liquid phase.

Streaming Potential

This phenomenon is opposite to electro osmosis. In this method by applying the pressure, the solution is passed through the membrane as a result of which a type of flow potential is incited. It is just proportional to the difference between pressure and the flow speed of the electrolyte solution through the membrane pores.

Sediment Potential

This phenomenon is opposite to electrophoresis. In this the movement of charge particle is measured under the influence of gravitation or sedimentation field in centrifuges. It is rarely used in the study of electro kinetic phenomena because it is very difficult to be measured.

Effect of Change of Zeta Potential Value on the Stability of System

Changes in stability of system due to changes in the value of zeta potential are given in Table 1.[21,22]

Table1. Change in the stability of system with change in value of zeta potential

Zeta Potential	Assessment of stability
From 0 to ±5	Rapid coagulation or flocculation
From ±10 to ±30	Incipient instability
From ±30 to ±40	Moderate stability
From ±40 to ±60	Good stability
More than ±61	Excellent stability

Patents on Zeta Potential

A List of some important patents on zeta potential is given in Table 2.

Table2. Patents on zeta potential

Patent No.	Title	Inventors	Year
3976852	Optimization petroleum recovery systems utilizing zeta potential[23]	Douglas, Larry J Wenger, Charles B	1976
7338808	Method and apparatus for determining zeta potential using alternating current electric field and T channel[24]	Cho, Yoon-kyoung Shin, Sang-min Kang, In-seok Lim, Geun-bae	2008
6325706	Use of zeta potential during chemical mechanical polishing for end point detection[25]	Krusell, Wilbur C. Nagengast, Andrew J Pant, Anil K	2001
8451434	Method and apparatus for measuring zeta potential of suspended particles[26]	Freud, Paul J Trainer, Michael N.	2013
8281662	Method for determining porosity, pore size and zeta potential of porous bodies[27]	Dukhin, Andrei Goetz, Philip J Thommes, Matthias	2012
4602989	Method and apparatus for determining the zeta potential of colloidal particles[28]	Culkin, Joseph B	1986
5686252	Immunoassay method utilizing zeta potential and immunoassay kit[29]	Nishizaki, Hiroshi	1997
7399549	Altering zeta potential of dispersions for better HCD performance and dispersion	O'Hara, Jeanette E	2008

	stability[30]		
8372434	Ophthalmic oil-in-water type emulsion with stable positive zeta potential[31]	Bague, Severine Philips, Betty Rabinovich-Guilatt, Laura Lambert, Gregory Garrigue, Jean-Sebastien	2013
8454837	Systems and methods for generation of low zeta potential mineral crystals to enhance quality of liquid solutions[32]	Bauer, Walter J	2013
20060175255	Systems and methods for generation of low zeta potential mineral crystals and hydrated electrons to enhance the quality of liquid solutions[33]	Bauer, Walter J	2006
7547413	Systems and methods for disinfecting and sterilizing by applying steam vapour containing low zeta potential mineral crystals[34]	Bauer, Walter J	2009
20060177342	Systems and methods for disinfecting and sterilizing by applying steam vapour containing low zeta potential mineral crystals[35]	Bauer, Walter J	2006
20070248645	Ophthalmic Oil-in-Water Type Emulsion with Stable Positive Zeta Potential[36]	Bague, Severine Philips, Betty Rabinovich-Guilatt, Laura Lambert, Gregory Garrigue, Jean- Sebastien	2005
8354462	Heat stabilizers containing hydrotalcite particles with specific zeta potentials that demonstrate improved processing and performance in molded vinyl compounds[37]	Baker, Paulette Pelzl, Bernhard Georg Schrunner, Herbert	2013

Applications of Zeta Potential

The physical properties of colloids and suspensions are totally dependent on the nature and extent of the particle- liquid interface which means that the behaviour of aqueous dispersions depends upon electrical and ionic structure of the interface. The production and stability of colloids and suspensions are both intimately related to electrical double layer that characterizes the interface. Zeta potential measurements are directly related to the nature and structure of the electric double layer at the particle-liquid interface. Zeta potential measurement is a key factor in the following areas:

Biomedical

Micro electrophoresis is a most useful technique for characterizing the surface of organisms such as bacteria, blood cells, viruses etc. In addition to chemical methods of analysis which can disrupt the organism, zeta potential measurement has given the information about the outermost regions of organisms. The main constituents of biological material (protein, lipid, polysaccharide, nucleic acid) show characteristic charge behaviour.

Clay Technology

The physical properties of clay-water systems such as sedimentation, filtration, swelling, viscosity, yield stress and structural strength are sensitive to the nature of the electric double layer surrounding the particles and if not have sufficient zeta potential the particles will aggregate. Zeta potential measurement provides particularly relevant information where colloid stability and/or ion adsorption is involved. Using the additives in the liquid phase control the behaviour of clay suspensions and also help in soil treatment, oil well drilling, ceramic and other processes involving clay like materials.

Water Purification and Industrial Waste Treatment

Municipal water supplies are generally obtained from sources that are contaminated with materials (both mineral and organic in nature) imitative from soil, domestic sewage and industrial waste. To facilitate the filtration of these contaminants, small quantities of flocculating agents are used. Electrophoretic measurements play an important role in the study of flocculation process. Before being discharged into streams industrial and mining; waste are also treated by the addition of coagulating additives to accelerate settling of suspended matter.

Detergency

The important factor in detergency is the prevention of dirt re-deposition after its removal. Re-deposition is governed by the influence of detergent adsorption, not only on the zeta potential of the dirt particles, but also on the zeta potential of the fabric surface.

Paints

The degree of dispersion of finely divided material has greater importance in the paint industry. The degree of dispersion can dominantly affects the colour quality, the gloss and the texture and flows. Increased homogenous dispersion increases brightness and glosses and gives a marked decrease in haze (diffuse reflection). Bronzing occurs only at coarse levels of dispersion, but not reveal at finer levels. Electrophoretic measurements under various conditions of composition, particle size and additives are useful in establishing optimum dispersion characteristics and the development of product that have wide acceptability.

Electrodepositon

Electrodepositon has major application in automobiles in painting of metal object such as automobiles bodies to prevent from corrosion. The metal article to be painted is made the anode and the container the cathode. When a suitable voltage is applied, negatively charged paint particles are deposited to the bodies from a moderately aqueous suspension, as a coherent film. The process is, in essence, an electrophoretic phenomenon in which the colloidal paint particles move through the aqueous electrolyte to the automobiles bodies being painted due to effect of the electric double layer. Electrophoretic mobility measurements are valuable in establishing the optimum pigment dispersion with various additives. Alkyls, epoxies, melamines, acrylics and other functional groups have been employed in formulation of paint for different electrocoating purposes.

Paper

Electrophoretic mobility measurements are revealed in investigating the effect of various coating ingredients, singly or in combination, on the rheology of the system. There is evidence that the charge on the particles controls the rheology more strongly.

Pharmaceuticals

One of the most difficult problems face in the pharmaceutical industry is the preparation of physically stable dispersions of a drug in a suitable suspension vehicle. A stable dispersion revealed no flocculation. The stability of parenteral and oral drugs in aqueous suspensions affects both dosage requirements and shelf life. Caking properties of pharmaceutical is also studied with the help of electrophoretic measurement.

Purification

Zeta potential measurements are useful in maintaining the optimum conditions for purification in a various chemical processes such as removal of impurities from sugar cane juice by precipitating an inorganic material which serves to collect the impurities and it can be achieved by determination of the proper zeta potential .

CONCLUSION

Zeta Potential (ζ) measurement is a very useful technique that gives information about the material surface- solution interface. Zeta Potential is used in understanding and controlling the stability of suspensions and emulsions; measurement of Zeta Potential is often the key in understanding dispersion and aggregation processes. By revealing the zeta potential we can determine the presence or absence of charge moieties on the surface material. The sign and magnitude of ZP affects process control, quality control, maintaining a more consistent product and also help to improve product quality and performance.

DECLARATION OF INTEREST

It is hereby declared that this paper does not have any conflict of interest.

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