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Research Article

Preparation and characterization of nimesulide loaded cellulose acetate hydrogen phthalate nanoparticles by salting out technique

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ABSTRACT

The aim of this study is to prepare nimesulide loaded cellulose acetate hydrogen phthalate nanoparticles by salting out technique. In this study Cellulose acetate Hydrogen phthalate was taken as polymer. Nimesulide was selected as a model drug. This technique is suitable for drugs and polymers that are soluble in polar solvents such as acetone or ethanol. The effect of drug concentration and polymer concentration on nanoparticle size, shape, uniform size distribution and stability was studied. Nanoparticles were evaluated for particle size, zetapotential and particle size distribution. Size of the particle was measured by SEM.(Scanning electron microscope).Surface charge and stability of the resultant nanoparticles was determined by Zetasizer. Particle size distribution was determined by Photon Correlation Spectroscopy (PCS) with a Malvern Zetasizer Nano-ZS. The cellulose acetate hydrogen phthalate concentration and nimesulide concentration was varied from 5mg/ml to 10 mg/ml. The effect of drug and polymer concentrations on nanoparticle size, shape, particle size distribution was studied. Increased drug concentration has no impact on the particle size. The size of the particle was found to be decreased with increased polymer concentration. Increased polymer concentration has resulted in uniform particle size distribution. Higher the polymer concentrations and lower the drug concentrations resulted in uniform particle size distribution.

Key words: Cellulose acetate Hydrogen Phthalate, Nimesulide, Zetapotential Scanning electron Microscope, Photon correlation spectroscopy, Zetasizer

INTRODUCTION

Nanoparticles are sub nanosized colloidal structures made up of synthetic and semisynthetic polymers. Several methods exist for the preparation of nanoparticles from biodegradable polymers [1,2].These include: emulsification solvent evaporation, monomer emulsion polymerization, salting out, and nanoprecipitation [3,4]. Depending on the preparation method drugs or antigens can either be entrapped in the polymer matrix, encapsulated in a liquid core, surrounded by a shell-like polymer membrane, or bound to the particle surface by adsorption [5,6]. For drug loading of nanoparticles, three major strategies can be employed: (1) covalent attachment of the drug to the particle surface or to the polymer prior to preparation, (2) adsorption of the drug to a preformed carrier system, and (3) incorporation of the drug into the particle matrix during particle preparation [7,8].

Nanoparticle preparation using polymer precipitation methods: In these hydrophobic polymer and a hydrophobic drug is dissolved in a organic solvent followed by its dispersion in a continuous aqueous phase in which polymer is insoluble. The external phase also contains stabilizer. Depending upon solvent miscibility techniques they are designated as solvent extraction/evaporation method [9,10].

The polymer precipitation occurs as consequence of the solvent extraction/evaporation at which can be brought by

a) Increasing the solubility of the organic solvent in the external medium by adding an alcohol (i.e isopropronolol)

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b) By incorporating additional amount of water into the ultra emulsion
c) By evaporation of organic solvent at room temperature or at accelerated temperature or by using vaccum. [11,12].
d) Using an organic solvent that is completely soluble in the continuous aqueous phase-nanoprecipitation [13].

Salting out: It is one of the most commonly adopted methods to prepare nanoparticles. The method involves the incorporation of saturated aqueous solution of polyvinylalcohol into an acetone solution of polymer under magnetic stirring to form an o/w emulsion [14,15]. The process differs from nanoprecipitation technique as in the latter the polymeric solution is completely miscible with the external aqueous medium. But in salting out technique, the miscibility of both phases is prevented by the saturation of external aqueous phase with PVA [16,17].The precipitation of polymer occurs when sufficient amount of water is added to external phase to allow complete diffusion of acetone from internal phase into aqueous phase. This technique is suitable for drugs and polymers that are soluble in polar solvents such as acetone or ethanol. [18,19]

MATERIALS AND METHODS

Materials: Cellulose acetate hydrogen phthalate Supplied by SD-Fine chemicals, Acetone Supplied by SD-Fine chemicals, Polyvinylalcohol supplied by Hi-Chem laboratories, Nimesulide Supplied by sigma laboratories and Magnesium chloride Supplied by SD-Fine chemicals

Methodology: Cellulose acetate Hydrogen phthalate polymer and nimesulide were dissolved in acetone. Polyvinylalcohol was dissolved in aqueous phase. Magnesium chloride was added to aqueous phase. The aqueous phase was added to organic phase under magnetic stirring at 700 rpm. Stirring was continued for 8 hrs. Finally water was added to precipitate nanoparticles. The emulsion was centrifuged at 13,000 rpm for 30 minutes. Finally the particles were dried at room temperature. Experiments were performed by changing the Drug concentration and keeping all the remaining parameters constant. The same experiment was repeated by changing the polymer concentration and keeping the remaining parameters constant [14]. The effect of drug concentration and polymer concentration on nanoparticle size, shape, particles distribution was studied.

RESULTS

Determining the size of nanoparticles: Size of nimesulide loaded CAHP nanoparticles was determined by scanning electron microscope. In order to perform the SEM observation, nanoparticle suspension was fist diluted with ultrapure water (1/5), and then a drop of the diluted nanoparticle suspension was then directly deposited on a polished aluminum sample holder. Samples were dried in vacuum. The morphology of nanoparticles was observed at 15 kV using a scanning electron microscope (SEM; S-3700 N, Hitachi, Japan).

Particle Size Analysis: Mean particle size of the nanoparticles was determined by Photon Correlation Spectroscopy (PCS) with a Malvern Zetasizer Nano-ZS (Malvern Instruments, Malvern, UK). Measurements were realized in triplicate at a 90º angle at 25ºC under suitable dilution conditions. Particle size distribution was expressed as mean diameter (nm) ± standard deviation and polydispersity index. Mean particle size was found to be 548.2 nm.

DISCUSSION

In this study, nimesulide was encapsulated into cellulose acetate hydrogen phthalate nanoparticles via salting out method. Here the effect of polymer (cellulose acetate hydrogen phthalate) concentration on the particle size was studied. The cellulose acetate hydrogen phthalate concentration was varied from 5mg/ml to 10 mg/ml. At 5 mg/ml concentration the particle size varied from 100nm to 200nm.When the concentration of cellulose acetate hydrogen phthalate has increased from 5 mg/ml to 10 mg/ml the particles were distributed in between 100-120nm. Then the effect of Drug(Nimesulide) concentration on the particle size was studied. The nimesulide concentration was varied from 5 mg/ml to 10 mg/ml. At 5 mg/ml concentration the particles were very tightly packed and distributed in between 100-200 nm. When the concentration of nimesulide has increased from 5 mg/ml to 10 mg/ml there was no difference in the particles size distribution. Particles were distributed in between 100 to 200 nm. Increased drug concentration has no impact on particle size. Finally particles were uniformly distributed at 10 mg/ml polymer and 5 mg/ml drug concentration. Mean particle size of the nanoparticles was determined by Photon Correlation Spectroscopy (PCS) with a Malvern Zetasizer. Mean particle size was found to be 548.2 nm. Zeta potential of nanoparticle dispersions was measured in mV by Malvern Zetasizer. Zetapotential of the nimesulide loaded Cellulose acetate hydrogen phthalate nanoparticles was found to be -19.8 mV indicating good stability.

CONCLUSIONS

Here the effect of drug, polymer concentrations on the particle size distribution was studied. Increased

drug concentration has no impact on the particle size. The size of the particle was found to be decreased with increased polymer concentration.Increased polymer concentration has resulted in uniform particle size distribution. Higher the polymer concentrations and lower the drug concentrations results in uniform particle size distribution. From the zetapotential report the resultant nanoparticles were found to be stable.Mean size of the particle was found to be 548.2 nm. Further study can be done on entrapment efficiency and drug release from polymeric nanoparticles.

ACKNOWLEDGMENTS

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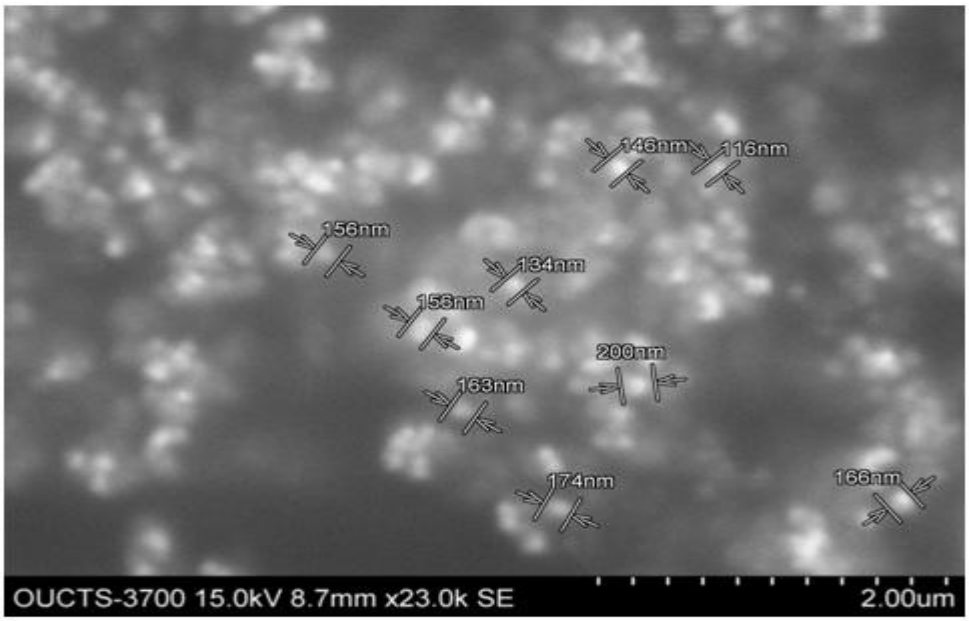

Figure 1: SEM images of Nimesulide loaded Cellulose acetate Hydrogen Phthalate nanoparticles (5mg CAHP,5 mgNM)

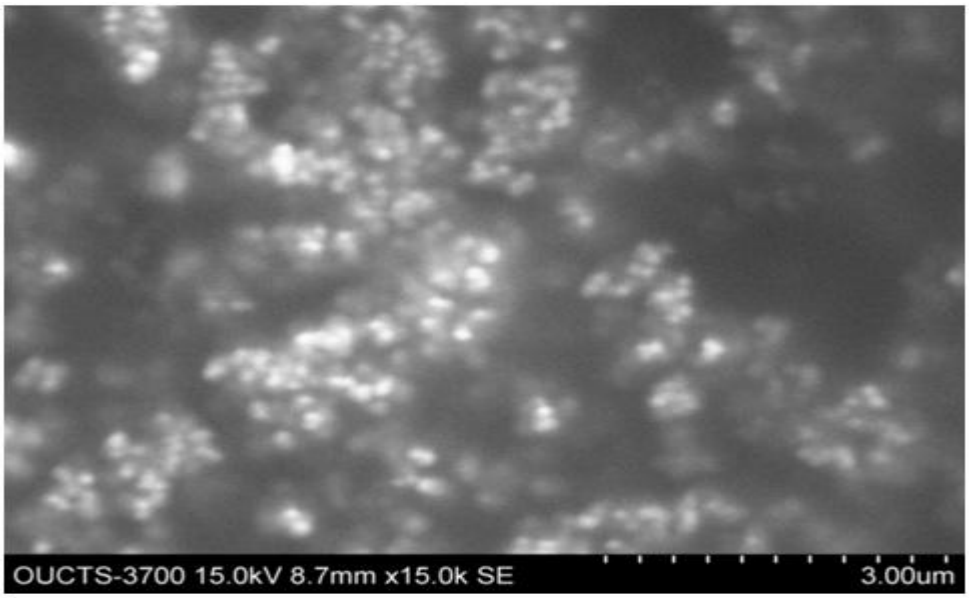

Figure 2: SEM images of Nimesulide loadedCellulose acetate Hydrogen Phthalate nanoparticles (5 mg, CAHP,5 mg NM)

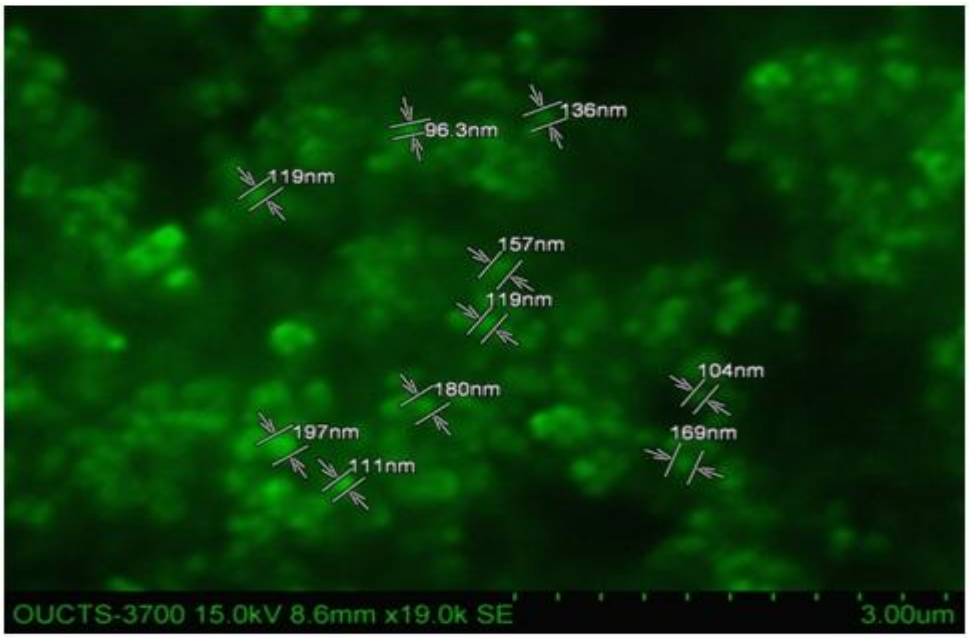

Figure 3: SEM images of Nimesulide loaded Cellulose acetate Hydrogen Phthalate nanoparticles (5 mg CAHP, 10 mg NM)

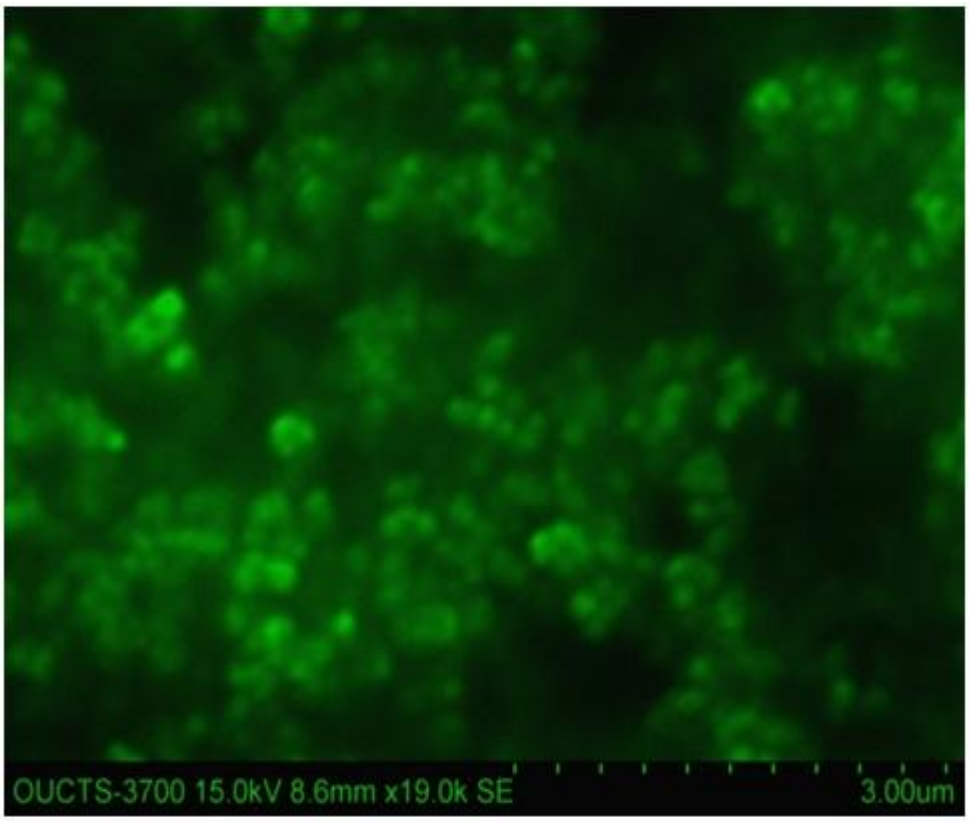

Figure 4: SEM images of Nimesulide loaded Cellulose acetate Hydrogen Phthalate nanoparticles (5 mg CAHP,10 mg NM)

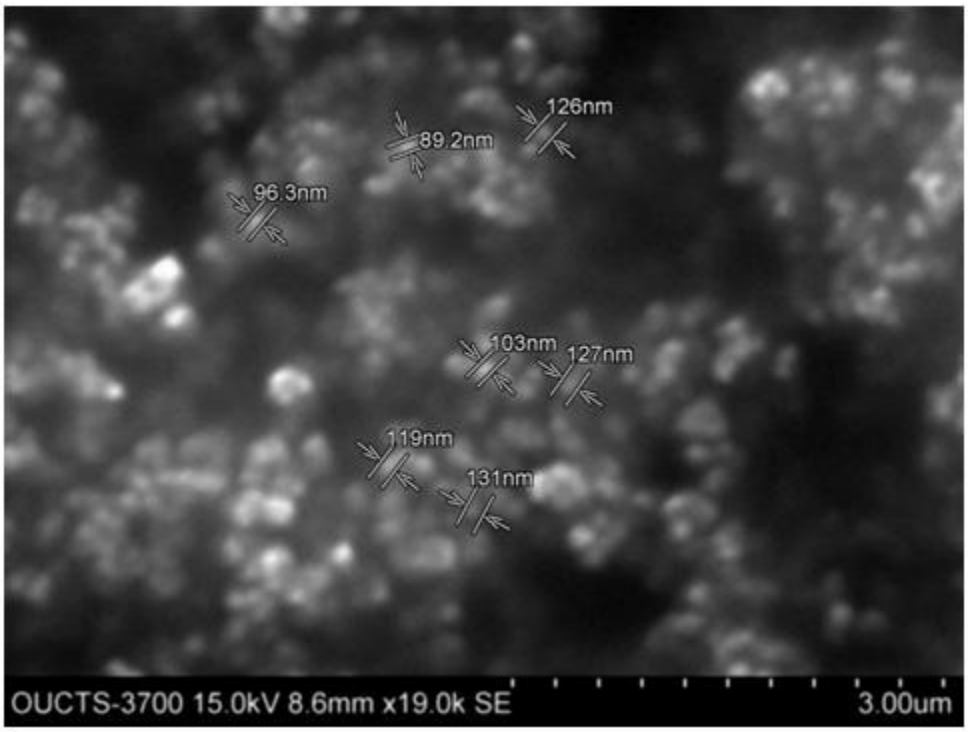

Figure 5: SEM images of Nimesulide loaded Cellulose acetate Hydrogen Phthalate nanoparticles (10 mg CAHP,5 mg NM)

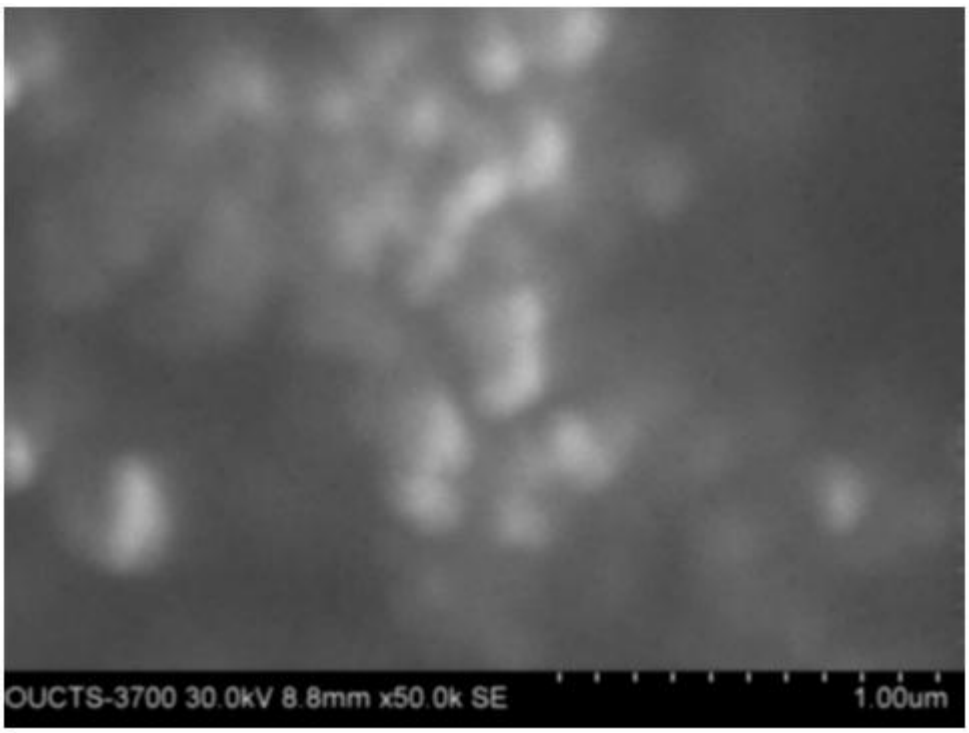

Figure 6: SEM images of Nimesulide loaded Cellulose acetate Hydrogen Phthalate nanoparticles (10 mg CAHP,5 mg NM)

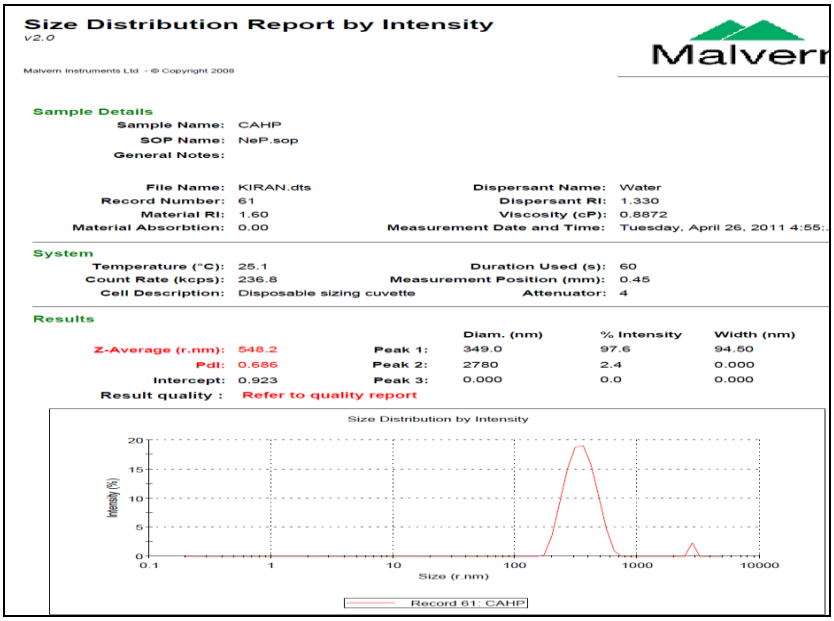

Figure 7: Size distribution by intensity

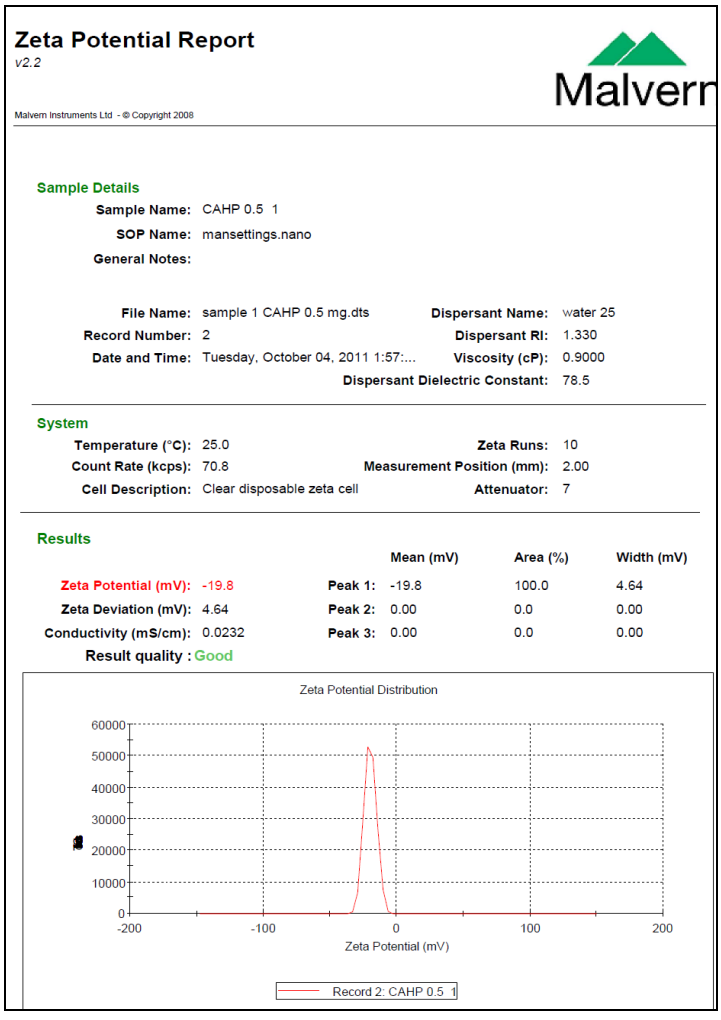

Figure 8: Zeta potential report

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