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# Stable aqueous film coating dispersion of zein

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## Abstract

The effects of plasticizers, pH, and electrolytes on film formation and physical stability of aqueous film coating dispersions (pseudolatexes) of zein were evaluated. The influence of plasticizer on film formation mechanism and minimum film-formation temperature (MFT) were monitored by means of hot stage microscopy (HSM). Furthermore, the effects of pH and electrolytes on the short-term physical stability of pseudolatexes were investigated by measuring relative absorbance, zeta potential, and particle size of the dispersions. With aqueous coating dispersions of zein, stages of film formation were identified. The dispersions plasticized with 20% (w/w) PEG 400 or glycerol formed mechanically strong and flexible films with the lowest glass transition temperature ($T_g$). Physical stability of the aqueous zein dispersions was dependent on both pH and electrolyte content. At a pH ranging from 3 to 4, the aqueous dispersions of zein were stable for at least 2 months exhibiting the highest values for zeta potential, the smallest particle size, and a low volume of aggregates. The stable dispersion could be obtained containing a lower concentration of electrolytes (e.g., $10^{-5}$ M). The physical stability of aqueous zein dispersions can be determined by the combined measurements of relative absorbance, zeta potential, and particle size.

*Keywords:* Zein; Aqueous dispersion; Film formation; Plasticizers; pH and electrolytes; Physical stability

## 1. Introduction

Aqueous polymeric dispersions (i.e., latexes and pseudolatexes) have been extensively used for the film coating of pharmaceutical solid dosage forms. These film coatings can be applied for uses such as protecting active pharmaceutical ingredients (APIs) from environmental light exposure, moisture, and oxygen, and/or masking unpleasant taste. Functional film coatings are used to impart site-specific (enteric) or controlled-release properties of oral medicines. Aqueous-based coating systems have numerous advantages over organic solvent-based systems with respect to ecological, toxicological, and manufacturing safety concerns [1].

Aqueous polymeric dispersions are increasingly used because of advantages such as low viscosity (even at a high solid content), low tackiness, and reduced coating times.

Aqueous dispersion of a film former is generally applied to a dosage form by the spraying technique. An important issue in this aqueous coating process is whether the aqueous dispersion is physically stable. An unstable dispersion results in aggregation of the colloidal particles, thereby affecting the film coating process. The aggregation process is complex, as it depends on a number of physical and chemical parameters (temperature, pressure, concentration, ionic force, pH, addition of denaturants, etc.) [2,3]. The stability of polymer dispersion is dependent on the size and surface charge of the colloidal polymeric particles as well as the composition and pH of the medium [4]. The addition of electrolytes or polymeric acids to the aqueous latex dispersion have recently been investigated to develop sustained release or time-controlled release dosage forms [5]. However, the addition of electrolytes or altering the pH affects the stability of colloidal dispersions.

Zein, an alcohol soluble protein made from corn, exhibits hydrophobic properties and low water uptake. Consequently, zein has been used as a film former for the controlled-release of APIs in pharmaceutical tablets [6] and masking the taste of bit-

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ter orally administered drugs [7]. To date, zein has been widely studied as a film former [8–11], but all of those studies mentioned above were related to organic-solvent-based films. There was only one study related to aqueous zein pseudolatex [12]. However, the characteristic brittleness of zein diminishes its usefulness as a film [13]. Propylene glycol, triethyl citrate and PEG 8000 were found to be compatible with zein pseudolatex. Upon drying, both the PEG 8000 and the triethyl citrate separated from the film. Propylene glycol remained incorporated in the film, but the tablet and bead coating with this pseudolatex revealed numerous surface defects and cracking in the film structure. It was also noted that zein pseudolatex began to display aggregation due to the formation of mold colonies [12]. In solution, zeins became an extended structure. It is well known that these proteins are organized in oligomers, which are resistant to high temperatures and treatment with reducing reagents and they tend to form high molecular weight (HMW) aggregates [14].

The aim of the present study was to investigate and gain understanding of the effects of plasticization, pH, and electrolytes on film formation and physical stability of aqueous film coating dispersions (pseudolatex) of zein. The stability mechanisms of dispersion were also investigated by the simultaneous analysis of the relative absorbance, electrokinetic properties, and particle size of the dispersion.

## 2. Materials and methods

### 2.1. Materials

The following chemicals were obtained from commercial suppliers and used as received: zein (Bache Pharmaceutical Co., Wujiang), glycerol (Ph. Eur.), castor oil (Ph. Eur.), polyethylene glycol (PEG 400; Fluka Chemie GmbH, Germany), natrium chloride (Ph. Eur.) and anhydrous calcium chloride (Fluka Chemie GmbH).

### 2.2. Methods

#### 2.2.1. Preparation of free films

The zein was dissolved in 70% ethanol and mixed for 30 min, then added to the same volume of water. The 10% zein dispersion was formed and continually stirred for several minutes, then filtered. The plasticizer was added at 10 and 20% (w/w, calculated from the polymer weight), respectively. The 6 ml of zein dispersion was taken and carefully dispersed to Teflon mould. The zein film was obtained by putting the mould containing zein dispersion into a 60 °C oven and dried for 4–12 h. The zein film was stabilized at 50 ± 5% RH at room temperature (20 ± 0.5 °C) for three days before the tests.

#### 2.2.2. Hot-stage microscopy (HSM)

The effects of plasticizers on film formation were monitored using a hot-stage microscope (Leica Microscopie and Systeme GmbH, Wetzlar, Germany). One drop of the dispersion was dripped onto the glass slide and spread thin. Measurements were performed at 60 and 75 °C respectively at 10 min heating period.

#### 2.2.3. Scanning electron microscopy (SEM)

The cross sections of free films were studied by scanning electron microscopy (SEM). SEM samples were prepared by attaching the free films to double-sided carbon tape and coated 20 nm platinum with a sputter coater (Agar sputter coater B7340, Agar Scientific Ltd., Stansted, UK). The micrographs were taken with a Zeiss DSM 820 (Carl Zeiss, Oberkochen, Germany). An accelerated voltage of 10 kV and secondary electrons were used for all micrographs.

#### 2.2.4. Mechanical properties

The mechanical and stress-strain properties of free films were determined using a Lloyd LRX materials testing machine (Lloyd Instruments Ltd., UK). For testing, the thickness of each film was measured at least at nine different points and the films were cut into strips. Dimensions of the strips were 9 × 1.5 cm. The strips were fixed into the grips of an apparatus and measurements were performed using a 100 N load cell, an initial gauge length of 6.0 cm and a crosshead speed of 5 mm/min. For each sample, elongation, yield stress, tensile strength and modulus of elasticity (Young's modulus) were calculated from the tensile-extension curve. The six parallel tests were determined for each sample.

#### 2.2.5. Glass transition temperature

The glass transition temperature ($T_g$) of zein powder and films were measured using a differential scanning calorimeter (Model 910 DSC, TA Instruments, New Castle, DE). Each film sample was accurately weighed in an aluminum pan before testing. The sample was heated from 0 to 300 °C at a rate of 10 °C/min.

#### 2.2.6. Stability studies

*2.2.6.1. Sedimentation study* The 5% zein dispersion was prepared. The dispersion in 10 ml cylinders was placed in a 25 °C bath. The sedimentation and separation of the dispersions were observed over time at different pH and electrolyte concentrations.

*2.2.6.2. Absorbance of dispersion* The zein dispersion has a maximum absorbance at 202 nm. UV spectrophotometer (UV2102 PCS, UNICO, Shanghai, China) was used to determine the absorbance of zein at 202 nm. The standard curve of zein dispersion was determined. The regression equation $A = 0.0528 + 0.0158C$ ($r = 0.9919$) was obtained using linear regression analysis. The effects of pH and electrolyte concentration on the stability of the latex dispersion were evaluated by measurement of $A/A_0$ changes with time ($A_0$ is the absorbance of dispersion at time zero; $A$ is the absorbance of dispersion at time $t$).

A 1% zein dispersion was prepared. The absorbance after centrifugation was determined by measuring the changes of light density after centrifugation. It expresses as

$$k = (I_0 - I)/I \times 100\%,$$