# Bottom up assembly of copolymer stabilised aqueous anthraquinone nanoparticles

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## Abstract

*Here we report recent developments in the stabilisation and delivery of hydrophobic crystalline dyes nanoparticles, into novel aqueous inkjet colorants. For the manufacture of stable nanoparticles two aspects are considered and controlled; generation of small particle size colorant by careful control of precipitation conditions in the 20 – 100 nm size range, and subsequent stabilisation of precipitated colorant by surfactant and/or copolymer. Colorant precipitation involves the initial creation of crystal nuclei, and their subsequent growth. Formation of stable nanoparticles with the smallest particle size requires a high nucleation rate but a low growth rate so as to avoid Ostwald ripening. Both process rates are dependent upon temperature and degree of supersaturation. Here we report the synthesis of copolymer stabilised anthraquinone nanoparticles using evaporative precipitation from dichloromethane into water. Copolymer stabilised dye nanoparticles in the 100nm size range are demonstrated and the role of copolymer on nanoparticle stabilisation and morphology discussed.*

## Introduction

This paper describes recent developments [1,2] for the stabilisation and delivery of hydrophobic crystalline drugs, as nanosuspensions, into novel inkjet colorants. The target size regime is 20 – 100nm. This approach has several advantages with respect to the design of inkjet colorants namely the delivery of hydrophobic dyes using an essentially aqueous ink vehicle yielding text and image having improved resistance to environmental stress factors.

For the manufacture of nanosuspensions/ nanoparticles two aspects need to be considered and controlled:

1. Generation of small particle size colorant by careful control of precipitation conditions.
2. Stabilisation of precipitated colorant by surfactant and/or polymer.

Regards colorant precipitation there are two processes involved: the initial creation of crystal nuclei, and their subsequent growth. Formation of a stable nanoparticle with the smallest particle size requires a high nucleation rate but a low growth rate so as to avoid Ostwald ripening. Several processes have been assessed and evaluated:

1. Rapid nucleation by metering small amounts of a water-miscible organic solution of the colorant to the non-solvent water, under rapid mixing. This rapid dilution of solvent results in high-supersaturation conditions which cause spontaneous nucleation, a rapid decrease in local supersaturation and hence reduced growth rate [3].
2. Freeze drying an O/W polymer stabilised dispersion of colorant solution and subsequent re dissolution in water [4].
3. Generation of colorant-polymer stabiliser nanocomposites using microwave induced diffusion and subsequent dispersion in aqueous fluids [5].

Here we report the use of an evaporative precipitation technique involving the spraying of colorant solution in a volatile organic solvent into a temperature controlled aqueous solution in the presence of stabiliser with rapid solvent evaporation resulting in rapid colorant precipitation (Quasi-emulsion solvent diffusion (QESD) [6]).

## Experimental

### *Copolymer Library*

In defining our copolymer library we are led by well established and understood polymer design principles [7,8]. The library explores copolymers which contain only hydrophobic segments having an affinity for the pigment surface, and hydrophilic carboxylic acid segments which when ionised with triethylamine (TEA), provide the charge-based stabilization required to maintain a finely divided dispersion [9,10]. All copolymers have a $M_n \approx 13{,}000$ gmol$^{-1}$; Pdi $\approx 2.3$ whilst overall polymer hydrophobicity, as defined by a calculated Hansch Parameters (Log P) [11], spans the range of 0.54 to 3.75. All copolymers were synthesized using conventional free radical polymerisation in 2-propanol using Vazo 67 initiator at 83°C.

### *Anthraquinone Dye*

Throughout this study we have used 1-amino-4-hydroxy-2-[4-(1,1,3,3-tetramethyl-butyl)-phenoxy}-anthraquinone (figure1) a hydrophobic crystalline dye (Tm = 171.5 °C) both because of its low water solubility and good solvent solubility.

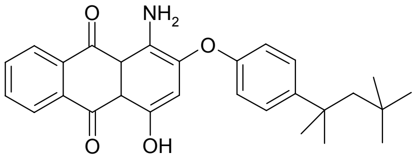

**Figure 1**: Anthraquinone Magenta H.110 300 dye.

### Dispersion Formulation

The following experimental setup was used through the study. 20 ml of dye solution was fed using a HP pump through steel tubing with an end tip diameter of 1/16 inch and internal diameter of 0.01 inches into 80ml of de-ionized water in a 250 ml round bottom flask equipped with thermometer, overhead stirrer and dean and stark condenser. The feed tip was placed 1cm below the surface of the water. Dye solution concentration, process temperature and feed rate are as discussed below.

### Dispersion Testing

Dispersion particle size were analysed directly without dilution using a Zetasizer Nano ZS from Malvern Instruments (PCS). Selected samples were analysed for particle size and morphology using Cryo Environmental Scanning Electron Microscopy (ESEM). This was done by first cooling the sample and introduction chamber of the ESEM to around -120°C. The sample was then placed in a brass tube and immersed in liquid nitrogen to freeze the solution in the tube. This tube was then placed in the introduction chamber and warmed up to around -90°C. The tube was then cut open around halfway up, exposing the frozen sample, which was then coated in a gold-platinum amalgam. The sample was then cooled down to -120°C and introduced to the viewing chamber, and viewed under an electron beam of 5-10 keV. Interaction between the polymer and dye in dispersions was evaluated by differential scanning calorimetry (DSC). Dispersions were dried into a 50µl aluminium DSC pan which was hermetically sealed. The pan was placed in a Perkin-Elmer Diamond DSC and scanned over a temperature range if 30-200°C at a prescribed heating rate.

## Results and Discussion

### Process Optimisation

The particle size and resultant stability of dye-copolymer nanoparticles prepared using an evaporative precipitation technique is highly process dependant. The following variables were found to be of primary importance, influencing directly particle nucleation rate and stabilisation:

Selection of volatile organic solvent.
Location and neutralization state of copolymer stabiliser.
Temperature of solution feed and aqueous dispersion.

and the following of secondary importance within the constraints imposed by the experimental design:

The feed rate.
Aqueous phase agitation.
The ratio of various components

Obviously these variables are not independent and therefore the following comments address only the key observations.

The requirements for a suitable volatile organic solvent are that it be a good solvent for both dye and stabilizing copolymer, have low water solubility and have a low boiling point such that on introduction to the aqueous phase the solvent is rapidly and efficiently removed. Dichloromethane (DCM) was found to best fit these selection criteria. Optimisation studies showed that pre-dissolution of the pre-neutralised polymeric stabiliser in dichloromethane with dye yielded the most stable nanosuspensions having the smallest particle size. This is believed to be due to the polymer-dye being in close admixture at the point of dye precipitation leading to rapid stabilisation so reducing the tendency towards Ostwald ripening. Similarly it was found that injecting the dye-polymer solution at a temperature just below the boiling point of dichloromethane into water held above the boiling point of dichloromethane (80$^{o}$C) resulted in rapid solvent evaporation and hence a high nucleation rate.

The feed rate of dichloromethane solution into water over the range 0.3-6 mlmin$^{-1}$ was found not to have an effect on dispersion particle size or stability. In order to minimise foam formation feed rates were kept below 2 mlmin$^{-1}$. Agitation of the aqueous phase using a four blade impeller rate at 250-500s$^{-1}$ was found to give reproducible results. Lower rates yielded larger particle size and higher rates foam formation problems.

The optimum ratio of dye-copolymer was 1:3 w/w. Further polymer added showed no improvement on dispersion properties, and a reduction showed an increase of dispersion particle size. The optimum ratio of organic solution added to aqueous solution was 20:80 respectively (v/v). The optimum ratio of dye: dichloromethane was found to be 0.5:80 respectively (w/w). This ratio could be increased to 5:80 with no loss in performance.

### Polymer Stabilisation

A single copolymer library was evaluated for there ability to stabilise dye-copolymer nanoparticles. This was made with a constant methacrylic acid (MAA) level of 17.5% w/w (98% neutralised with TEA), and varying the amounts of methyl methacrylate (MMA) and ethylhexylmethacrylate (EHMA) to vary the hydrophobicity of the copolymer over the Log P range of 0.54 to 3.75.

Mono-modal particle size for dye-copolymer nanoparticles at 1:3 w/w made from this library are summarised in Figure 2 with mono-modal particle size indicated in nm as measured by PCS. This shows a strong dependence of particle size on copolymer stabiliser composition with two identified sweet spots. The first at a copolymer composition of MMA/EHMA/MAA = 47.5/35/17.5 equates to an overall copolymer hydrophobicity of Log P = 2.0 and is consistent with earlier published data on general copolymer dispersant effectiveness [12]. The second local minima at MMA/EHMA/MAA = 7.5/75/17.5 equating to an overall copolymer hydrophobicity of Log P = 3.15 was unexpected with the composition thought to be too hydrophobic to act as an effective dispersant. The reason for this local minimum is as yet not fully rationalised but it is currently believed to represent a compositional region resulting in highly favourable dye: copolymer interaction.

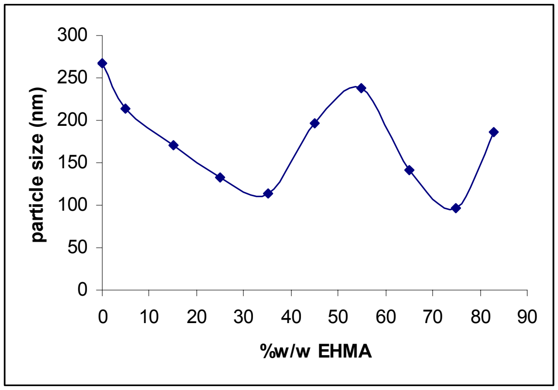

**Figure 2:** Effect of copolymer composition at constant MAA content (17.5 %w/w) versus dye-copolymer nanoparticle mono-modal particle size measure by PCS.

### *Particle Shape and Morphology*

Selected samples were examined under cryo-ESEM for particle size and shape analysis (Figure 3). These results confirmed that samples had slightly smaller diameter than determined by PCS and were essentially oblate in shape.

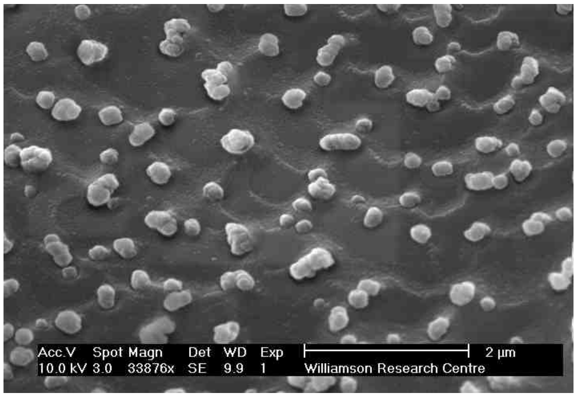

**Figure 3:** Cryo-ESEM image Anthraquinone Magenta H.110 300 and dye-copolymer (MMA/EHMA/MAA = 47.5/35/17.5) nanoparticles at 1:3 w/w ratio.

X-ray powder diffraction analysis of dye: copolymer samples were conducted under different drying and compositional regimes (Figure 4). These confirm that the nanoparticles contain both crystalline and amorphous dye.

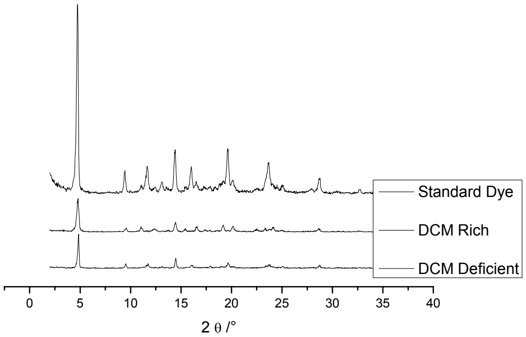

**Figure 4:** XRD powder diffraction of Anthraquinone Magenta H.110 300 and dye-copolymer (MMA/EHMA/MAA = 47.5/35/17.5) nanoparticles at 1:3 w/w ratio.

Through analysis of the melting point of pure dye and of solution cast dye-copolymer blends we observe that the measured enthalpy of fusion at the melting point ($\Delta H_{fusion}$ ($Jg^{-1}$)) is less than that calculated assuming full dye crystallisation at copolymer contents > 10 wt-% (Figure 5).

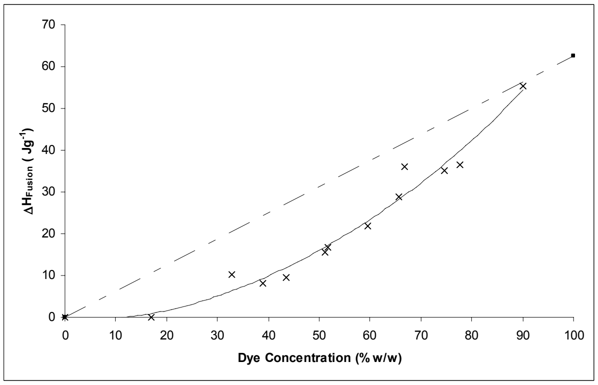

**Figure 5:** Enthalpy of fusion ($\Delta H_{fusion}$ /$Jg^{-1}$) determined by DSC run at 20 °C/min for dye-copolymer solution cast blends (-) and data calculated assuming full dye crystallisation (-.-).

For dye-copolymer (MMA/EHMA/MAA = 47.5/35/17.5) nanoparticle at 1:3 w/w ratio $\Delta H_{fusion}$ = 4 $Jg^{-1}$ indicating that only 25% of the available dye is in a crystalline form.

## Conclusions

Polymer stabilised aqueous hydrophobic dye nanoparticles in the 100nm size range prepared by an evaporative solvent technique are demonstrated. The nanoparticle morphology is consistent with domains of crystalline dye in an amorphous dye-polymer matrix. The degree of dye crystallisation within the nanoparticle is a function of the dye-polymer ratio with high copolymer fractions leading to low levels of dye crystallisation. Copolymer composition is critical with respect to nanoparticle stabilisation and the importance of favourable dye-copolymer interaction is demonstrated.

## Acknowledgements

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## Author Biography

*Professor Yeates has over 20 years industrial experience working for ICI, Zeneca and Avecia Ltd in the area of specialty polymer chemistry. During that time he held a number of senior technical positions developing and implementing research strategy. Over the last 7 years in industry he developed a particular interest in organic semiconductors and inkjet printing for both industrial and SOHO applications. In November 2004 he was appointed to the full time academic position as Professor of Polymer Chemistry, a Organic Materials Innovation Centre (OMIC) at the University of Manchester.*