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The influence of preparation parameters on size and charge distributions of poly (butylcyanoacrylate) nanoparticles evaluated by response surface modelling (RSM)

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Poly(butylcyanoacrylate) (PBCA) nanoparticles have been documented extensively as a sustained release, particulate drug delivery system. They display low toxicity, ideal biodegradability characteristics, an ability to incorporate a wide variety of drugs and represent a potential vehicle for drug targeting. The aim of this work was to investigate the influence of preparation factors on the size range, polydispersity, zeta potential and preparation efficiency from defined experimental conditions. Studies in process elucidation and optimisation vary one factor whilst keeping all other factors constant. This can be both inefficient and time consuming. Alternatively, a factorial design can be used, which enables the experimental responses to be collected with the minimum number of observations. The responses (dependant variables) are measured and analysed by carrying out multiple regression analysis and statistically significant terms are identified using analysis of variance (ANOVA).

In this work, a 3^3 full factorial design was carried out requiring 27 observations to be performed, each repeated a further four times. PBCA nanoparticles were prepared by adding monomer dropwise at a rate of 50 µl per minute to a stirring aqueous buffer (PBS, 25 ml) containing surfactant (Synperonic PE/F). The solution was allowed to stir for a further 2 hours to complete polymerization and filtered through sintered glass. The pH of the polymerization buffer, monomer concentration and surfactant concentration were considered to play a significant role in particle formation and, thus, selected as the independent variables (factors). Particle Z_{ave} , zeta potential, polydispersity, % preparation efficiency were chosen as the responses. The variance (n=5) in each response was determined from the replicate experiments and assigned as a further four responses.

Second-order models with interaction terms were found to best describe observations. The pH factor was highly significant ($p < 0.0001$) for influencing particle size, polydispersity, zeta potential and % recovery. The interaction term between pH and surfactant was also found to be significant for size, zeta potential and poly-dispersity ($p<0.05$). Monomer and surfactant concentrations were found to be significant ($p<0.05$) factors influencing the % recoveries. RSM was also used to model the relationship between the variance in each response to the experimental factors, as shown in Figure 1.

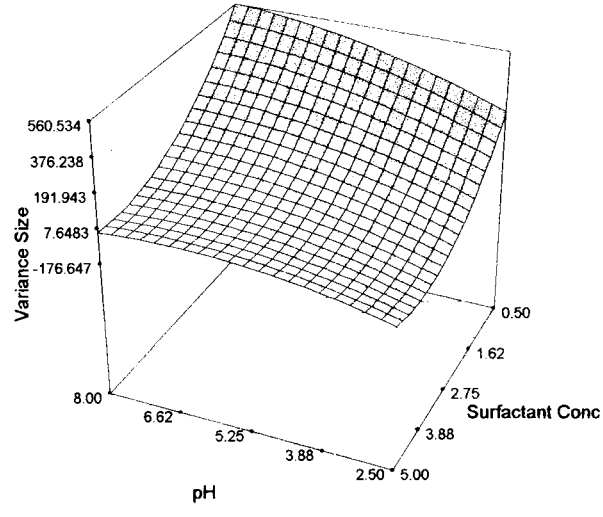

Figure 1 shows the response surface relating variance in particle size to surfactant concentration and pH.

Using RSM, it was possible to select regions in the experimental design where responses, such as particle size and zeta potential lie within a desired range. Furthermore, it was possible to identify regions where the variance was expected to be a minimum.