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EXPERIMENTAL DESIGN AND OPTIMIZATION OF HYDROGEL NANOPARTICLES PREPARATION USING IONOTROPIC GELATION METHOD

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Hydrogel nanoparticles (nanogels) are among the most promising nanoparticulate drug delivery systems owing to their small and controllable sizes, very high hydrophilicity, ease of preparation and handling and remarkable biocompatibility. This type of particles can evade reticulo-endothelial system (RES) and remain in blood circulation for long time due to their hydrophilicity and submicron size features. In this study, a simple method based on ionotropic gelation was set up and optimized for preparation of chitosan-based nanogels.

A three-step experimental design was used in developing a model for optimal nanogels preparation in this work. A 2^{8-2} fractional factorial design augmented with 7 center points revealed that pH of chitosan solution, Chitosan initial concentration, tripolyphosphate (TPP) initial concentration, addition time of TPP solution to chitosan solution and temperature were the most significant factors, whereas the other factors were not important within the levels tested. The methods of steepest ascent and descent were used to approach the proximity of optimum. This task was followed by a central composite design to develop a response surface for optimization of nanogels preparation. To confirm the model adequacy for predicting minimum particle size, three additional experiments using the optimum condition were performed.

The optimum condition for nanogels production was found to be: pH of chitosan solution 4.8, Chitosan concentration 0.12% (w/v), TPP concentration 1.17% (w/v), addition time of TPP solution to chitosan solution 1.52 min and temperature 10.33 ˚C. This condition was projected to produce, theoretically, nanogels with 283 nm diameter. Using this condition, an experimental minimum particle size of 250.87 ± 37.8 nm verified the applied methodology.

At last, the ionotropic gelation method was optimized for nanogel preparation with considerably less experimental effort, greater precision, and facilitated system modeling.