## L-Ascorbic Acid and Thymoquinone Dual-Loaded Palmitoyl-Chitosan Nanoparticles: Improved Preparation Method, Encapsulation and Release Efficiency

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Abstract: Encapsulation of dual compounds of different characters (hydrophilic and hydrophobic) in single nanoparticles carrier could reach the site of action more accurately with the synergistic effect but it is less investigated. In our previous findings, combined-compounds encapsulation and delivery from chitosan nanoparticles were impaired by the hydrophilicity of chitosan. Therefore, hydrophobic modification on chitosan with palmitic acid was conducted in this study to provide an amphiphilic environment for better encapsulation of antioxidants; hydrophobic thymoquinone (TQ) and hydrophilic L-ascorbic acid (LAA). Palmitoyl chitosan nanoparticles (PCNPs) co-loaded with TQ and LAA (PCNP-TQ-LAA) were synthesized via the ionic gelation method. Few characterizations were conducted involving nanosizer, Fourier-transform infrared spectroscopy (FTIR), field-emission scanning electron microscopy (FESEM) and high-resolution transmission electron microscopy (HRTEM). UV-VIS spectrophotometry was used to analyze the encapsulation and release efficiency of the compounds in PCNPs. Successfully modified PCNP-TQ-LAA had an average particle size of 247.7 ± 24.0 nm, polydispersity index (PDI) of 0.348 ± 0.043 and zeta potential of 19.60 ± 1.27 mV. Encapsulation efficiency of TQ and LAA in PCNP-TQ-LAA increased to  $64.9 \pm 5.3\%$  and  $90.0 \pm 0\%$ , respectively. TQ and LAA in PCNP-TQ-LAA system showed zero-order release kinetics, with a release percentage of 97.5% and 36.1%, respectively. Improved preparation method, encapsulation and release efficiency in this study are anticipated to be beneficial for polymeric nanocarrier development.

Keywords: chitosan; co-loaded nanoparticles; hydrophobic modification; L-ascorbic acid; thymoquinone

## SUPPLEMENTARY MATERIALS

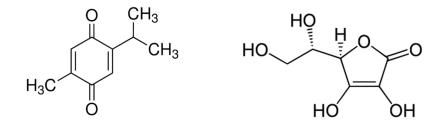


Figure S1: Chemical structure of thymoquinone, TQ (left) and L-ascorbic acid, LAA (right).