Influence of preparation parameters of M-InTBPPc-loaded PLGA-PEG nanoparticles on the entrapment efficiency and the residual PVA

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Keywords: *Phenoxy-phthalocyanine, Nanoparticle, PLGA-PEG, Entrapment Efficiency, PVA Residual, Factorial Design.*

Introduction

Drug delivery systems for photossensitizers have received attention due to literature results shown improvement in the efficacy of photodynamic therapy[1]. For this reason, the 2,3-(tetrakis[4-(benzyloxy)phenoxy]phthalocyaninato) indium (III) (M-InTBPPc) was encapsulated into nanoparticles of PEGylated poly(lactide-co-glycolide) (PLGA-PEG). Several factors involved in the nanoparticle preparation can influence the nanoparticulate properties that are fundamental for photosensitizer efficiency[2]. In view of this, the influence of PLGA-PEG concentration (Factor A), the acetone percentage in the organic phase (Factor B), the g force (Factor C) and time (Factor D) used in the centrifugation were evaluated on the entrapment efficiency and the residual percentage of poly(vinyl alcohol) (PVA) on the nanoparticles using a 2^4 factorial design with 16 experiments (32 replicates).

Results and Discussion

The entrapment efficiency was determined by quantification of M-InTBPPc present in the nanoparticles using a calibration curve. For this, a mass of lyophilized nanoparticles was dissolved in dimethylformamide (DMF) and the absorbance was measured in the wavelength with maximum intensity (693 nm). The experiment 1 presented the highest entrapment efficiency (89 ± 15)% and the experiment 16 the smallest (30 ± 4)%, disclosed that the conditions for experiment 1 was more adequated to obtain the best encapsulation of M-InTBPPc (not shown). Considering the Lenth's margin of error, factorial design disclosed that the individual factors B and D, and the combinatory effect (antagonic) of factors ABD and AB, decreased the entrapment efficiency (-15,69%, -11,56%, -14,19% and -12,69%, respectively) while the synergic effect of factors BD caused an increase (13,81%). Therefore, the factor B was the main paramater that influenced the M-InTBPPc entrapment (Figure 1). The acetone (Factor B) is a solvent that favors the M-InTBPPc diffusion from organic phase to aqueous phase, decreasing the entrapment efficiency of the photosensitizer. The centrifugation time (Fator D) also decreased the M-InTBPPc entrapment since the longer times recovered the smaller nanoparticles. Experiments have shown that there is an inverse relationship between the diameters of the nanoparticles and the entrapment efficiency (not shown).

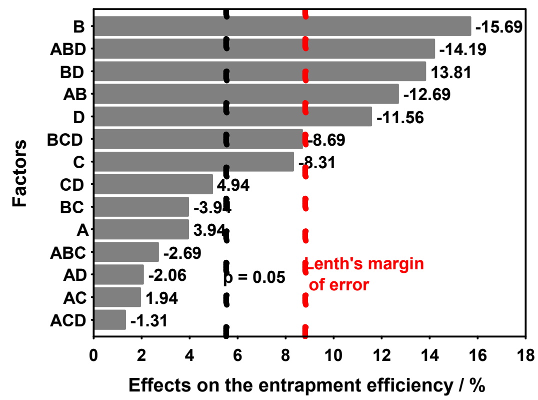

Figure 1 – Effect of factors A, B, C and D on the entrapment efficiency of M-InTPPc.

The residual PVA was determined by colorimetric method based on the interaction of PVA, boric acid and iodine. The experiment 3 presented the smallest percentage of residual PVA (0,05 ± 0,01)% (^{mass}PVA/^{m}Particle), while the experiment 14 the highest percentage (0,27 ± 0,03)%. Factorial design disclosed that the PLGA-PEG concentration was the more significant factor to increase the residual PVA (+0,12%) (not shown).

Conclusion

The main factors responsible for reducing the M-InTBPPc entrapment were Factors B and D. Factors A and C were responsible for increasing the residual PVA on the nanoparticle.

Acknowledgments

We thank FAPES and IFES for financial support.

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