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# Evaluation of bevacizumab activity during encapsulation into polymeric nanospheres by double emulsion method

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**Background and Aims:** Monoclonal antibodies (mAbs) are currently among the fastest growing classes of therapeutic entities. Owning to such efforts, adequate delivery systems to preserve their activity and control their release are required. Although injectable polymeric nanoparticles are among the best candidates to reach this purpose, antibody instabilities have been the major hindrance. Most of the papers in this field has just concentrated on structural stability of proteins loaded in polymers such as poly(lactic-co-glycolic) acid (PLGA) rather than their activity.
Methods: In this study we have investigated the activity of bevacizumab, a model antibody drug, during encapsulation into PLGA in presence and absence of stabilizers. Nanoparticles were prepared by double emulsion method. The effects of organic solvents, homogenization techniques and different stabilizers (mannitol, trehalose, glycine, PEG (300, 1000 and 4000 D), polysorbate 80, and bovine serum albumin (BSA), polyvinyl alcohol) on the activity of bevacizumab were evaluated by enzyme-linked immunosorbent assay (ELISA) and sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE), respectively.
Results: Results suggest that all of examined organic solvents cause a considerable reduction in antibody activity. Presence of interfaces between aqueous and organic phase, rather than shear stress during homogenizing, is the main reason of protein denaturation and inactivation in emulsion methods. Up to now, complete release of totally intact protein has not been achieved even in optimized encapsulation processes. We revealed that presence of 10% w/v BSA in internal aqueous phase during primary emulsification was an effective strategy to preserve the activity of bevacizumab.
Conclusions: Finally it can be concluded that this systematic process can be use to produce efficient sustained release nanoparticles for antibodies as well as other therapeutic proteins.

**Keywords:** PLGA nanospheres; Bevacizumab; Double emulsion; Stabilizer