Research in Pharmaceutical Sciences, 2012;7(5)
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Preparation and characterization of multivesicular vesicles (MVVs) containing gentamicin as a depot drug delivery system

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Background and Aims: Multivesicular liposomes (DepoFoam®) were composed of a set of closely packed non-concentric vesicles that confers an increased level of drug encapsulation, stability and longer duration release. Encapsulation of aminoglycosids into phospholipidic DepoFoam have been demonstrated improving effectiveness against microorganism and reduced in systemic toxicity. This is the first report demonstrating that nonionic surfactants could form MVVs for encapsulation of gentamicin.
Methods: Multivesicular vesicles were produced according double emulsification process. The first w/o emulsion was comprised gentamicin in the aqueous core, while the chloroformic solution contains phospholipid (DPPC or DMPC) or non-ionic surfactant (Span85, Span40, Span20, Tween65, Brij52), cholesterol, charged component (DCP or DPPG) and a triglyceride (triolein or Tripalmetin). The stable w/o emulsion was produced according RHLB determination. The second immiscible aqueous phase (having different tonicity) was added by mechanical mixing to form spherule dispersion (double emulsification). The spherules rearranged to MVVs after completely evaporation of the organic solvent by passing nitrogen over or through the dispersion. All MVVs were evaluated for their particle size and size distribution, morphology (optical microscopy and cryo-TEM), entrapment efficiency, in vitro drug release, and physical stability. Gentamicin was determined according in house validated HPLC analysis after derivatization by phenylisocyanate.
Results: The cryo-TEM images confirmed a set of closely packed non-concentric bilayer vesicles. MVVs were formed using nonionic surfactants of Span85-span40 with gentamicin encapsulation efficiency of 6-13%, while multivesicular liposomes comprised of DPPC-DMPC encapsulated more (6-25%). The encapsulated Gentamicin was released in vitro from the multivesicular liposomes during 75 hours according the first-order release kinetic.
Conclusions: MVVs comprised of both phospholipid and nonionic surfactants were developed successfully for the prolonged release of gentamicin. The DepoFoam technology is highly versatile and has been demonstrated to efficiently deliver several molecules in a sustained manner, including the gentamicin described here.

Keywords: Gentamicin; Multivesicular vesicle; DepoFoam; Non-ionic Surfactants; Phospholipid