ANTIOXIDANT PLGA NANOPARTICLES: PARTICLES WITH ENTRAPPED ALPHA-TOCOPHEROL VERSUS PARTICLES SYNTHESIZED WITH ALPHA-TOCOPHEROL-DERIVATIVE SURFACTANT

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Introduction

Natural antioxidants, including vitamin E (α-tocopherol), vitamin C and others have the ability to potentially modulate oxidative stress, responsible to some extent for diseases such as cancer and cardiovascular diseases. Natural antioxidants are prone to degradation and their bioavailability is limited by low absorption and degradation during delivery. Nanoparticles can offer several advantages over traditional delivery methods for antioxidants (Fig. 1), which include protection of the bioactive component from the environment [1-2], an increase in the bioavailability of the antioxidant [3], targeted delivery of the component, as well as its controlled release at the site of action [4-6].

Despite all these advantages, polymeric nanoparticles, in and of themselves, do not provide any benefits in the treatment of disease, but rather, they act as carriers for the drug. The next generation of nano drug delivery systems will need to be more proactive, able to "sense" the environment and react to the external stimuli in a controlled and expected way, which would result in a beneficial effect for the body. Not only will nanoparticles act as carriers, but also as active agents, participating in the overall health treatment.

We showed in prior work that functional surfactants with antioxidant properties can be used to form nanostructures of inherent antioxidant activity. The goal of this project was to compare antioxidant activity of poly(lactic-co-glycolic) acid (PLGA) nanoparticles with entrapped alpha-tocopherol against PLGA particles synthesized with aid from a functional surfactant of antioxidant activity made from α-tocopherol (vitamin E) and ascorbic acid (vitamin C), dubbed as EC.

Experimental

PLGA nanoparticles with entrapped alpha-tocopherol (PLGA(aT)) were made by emulsion evaporation [6] and PLGA-EC nanoparticles were made by nanoprecipitation [7]. The physical (size, size distribution, morphology) and antioxidant properties of the PLGA(aT) and PLGA-EC particles were measured by DLS, TEM, and DPPH respectively, and compared against each other.

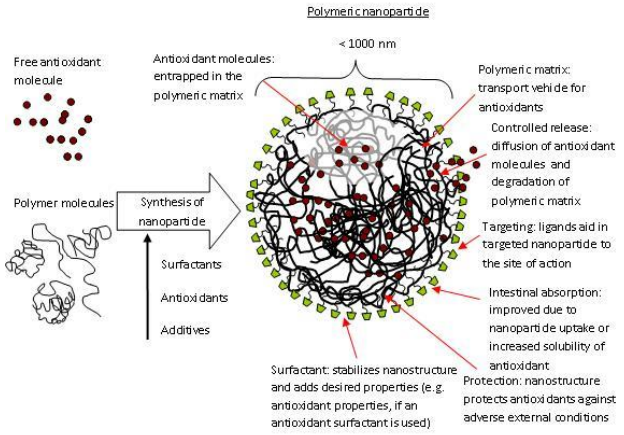

Fig. 1 Description of the nanoparticle antioxidant system with emphasis on the advantages offered by nanoparticle delivery systems

Results and Discussion

Spherical PLGA(aT) nanoparticles measuring 200 nm (Fig. 2a) were prepared with Polyvinyl alcoho) (PVA) as an emulsifier. No significant change in the PLGA(aT) size was observed with the entrapment of α-tocopherol at 0, 8, and 16% initial loadings. The polydispersity index after synthesis was 0.1 and zeta potential was negative for all nanoparticles (-29 mV for empty particles and -13 mV for loaded particles). The entrapment efficiency of α-tocopherol in the polymeric matrix was 89% for nanoparticles with 8% α-tocopherol theoretical loading and approximately 95% for nanoparticles with 16% α-tocopherol theoretical loading. DPPH data acquired for the 16% initial loading PLGA(aT) particles provided an IC50 (antioxidant concentration at which 50% inhibition is achieved) equivalent to 0.3 mg nanoparticles/ml or 39.6 mM when expressed relative to the amount of alpha-tocopherol present in the system.

In comparison, PLGA nanoparticles made by nanoprecipitation with the antioxidant EC as a

surfactant, measured 90 to 126 nm (Fig. 2b) at PLGA concentrations ranging from 40% to 120% w/w PLGA to surfactant, with an average polydispersity of 0.14. The IC_{50} of PLGA-EC were 41.1, 40.3, 41.1, and 39 mM for EC concentrations of 0, 40, 80, and 120% (PLGA:EC w/w %), respectively. The data suggested that the amount of PLGA, nanoparticle size, and PI did not affect the antioxidant properties of the PLGA-EC nanoparticles, which had an average IC_{50} of 40.4 µM (when expressed relative to the amount of EC present in the system) or 0.045 mg/ml when expressed in terms of nanoparticle concentration.

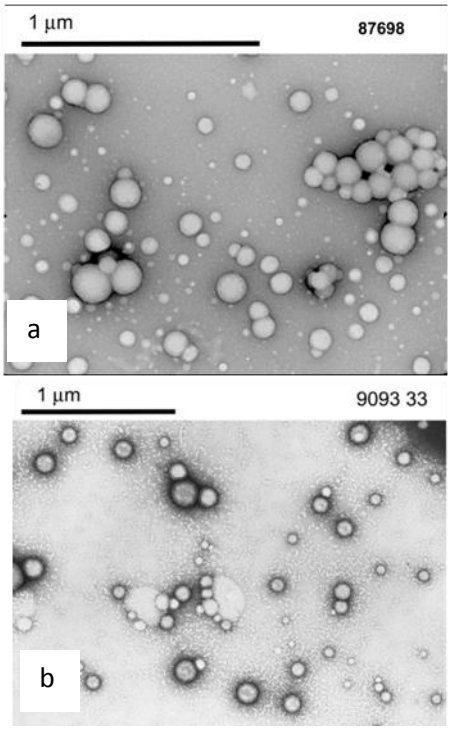

Fig. 2 TEM picture of nanoparticles prepared with a. PVA as an emulsifier and entrapped alpha-tocopherol at 16% initial loading (w/v % relative to PLGA), and b. EC as an antioxidant surfactant with 80% EC (w/v % relative to PLGA).

The IC50 of the PLGA(aT) and PLGA-EC were similar when expressed per mole of antioxidant (averaging 40 µM) and roughly twice the IC50 of ascorbic acid (vitamin C) or alpha-tocopherol (vitamin E). The different amounts of antioxidant entrapped in the PLGA matrix for PLGA(aT) nanoparticles (16% w/w relative to the polymer), respectively present on the PLGA particle surface, for PLGA-EC nanoparticles (80-250% w/w relative to the polymer), were responsible for better antioxidant activity of the PLGA-EC nanoparticles versus PLGA(aT) (IC50 of 0.045 mg/ml versus 0.3 mg/ml). This finding is of importance considering that the amount of alpha-tocopherol that could be entrapped in the PLGA matrix to form PLGA(aT) is limited, whereas much higher amounts of antioxidant could be delivered in form of a surfactant with PLGA-EC particles.

Conclusion

It is concluded that PLGA-EC particles formed with novel antioxidant EC surfactant is a valid alternative to PLGA(aT) particles for effective delivery of antioxidants necessary to combat oxidative stress and prevent cancer and cardiovascular diseases.

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