Loaded polymeric nanoparticles for drug delivery

Peres I., Rocha S., Pereira M.C., Coelho M.

LEPAE, Chemical Engineering Department, Faculty of Engineering, University of Porto, Rua Roberto Frias, 4200-465 Porto, Portugal

dce06013@fe.up.pt

Free radicals and oxidative stress are related to cancer, cardiovascular disease, diabetes, autoimmune disorders and neurological disorders (*1*). Epidemiological studies have shown that a diet enriched in antioxidants is associated with reduced risk of such disorders (*2*). Antioxidants, such as catechins from green tea, show a wide range of biological activities including antithrombotic, vasodilatory and anticarcinogenic effects, as well as anti-inflammatory, antiallergic, antiulcer, and antimicrobial properties (*3*). Catechins act as free radical scavengers and chelators of metal ions (*4*). Oral administration is the most efficient delivery system of antioxidants, however oral bioavailability of tea catechins is very low, less than 2-5% and their systemic clearance is also high (*5*). Encapsulation of catechins in carbohydrate nanoparticles (*6*) or other pre-formed materials (*7*), represents a solution to increase the antioxidant's efficacy of therapy. Spray-drying technology is widely used for drying biomolecules or colloidal particles and is based on a fast (~10 sec) convective drying process, in which hot air provides energy for evaporation of solvent (water) from liquid drops formed by atomization. Mixtures of gum arabic and maltodextrin have shown promise as high solid carriers, giving acceptable viscosity in studies on microencapsulation of cardamom oil by spray-drying (*8*). In this work, gum arabic-maltodextrin particles loaded with EGCG (EGCG/P) were successfully produced by homogenization and spray-drying, with an EGCG loading efficiency of 96±3%. Spray-dried particles are spherical or corrugated and polydisperse. The particles in aqueous suspension by dynamic light scattering (DLS) revealed two main populations, with mean average diameters of 40 nm and 400 nm (Figure 1). Transmission electron microscopy (TEM) images (Figure 2) corroborate de DLS measurements. Attenuated total reflection-infrared spectroscopy (ATR-IR) confirmed that EGCG was incorporated in the carbohydrate matrix by intermolecular interactions, maintaining its chemical integrity. Atomic force microscopy imaging proved the particle spherical shape, size and resistance to mechanical strength (up to 8 MPa). Nuclear Magnetic Resonance spectroscopy (NMR) experiments, have been performed to determine the structure of the epigallocatechin gallate-polysaccharide conjugates and to clarify the mechanisms of drug immobilization into the polymer matrix (Table 1). The results suggest the entrapment of EGCG into the polysaccharide matrix of maltodextrin/gum arabic (MD/GA) and support the potential of these vehicles for their sustained delivery and release. This study highlights the use of polysaccharide nanoparticles in chemoprevention as they can be used to deliver natural antioxidants capable of inhibiting steps of the tumorigenesis process in prostate cancer cell lines (Du 145). The results achieved, demonstrate that the carbohydrate matrix is able to preserve EGCG antioxidant properties, as proof of concept to be used as polymeric drug carrier.

References

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Figures

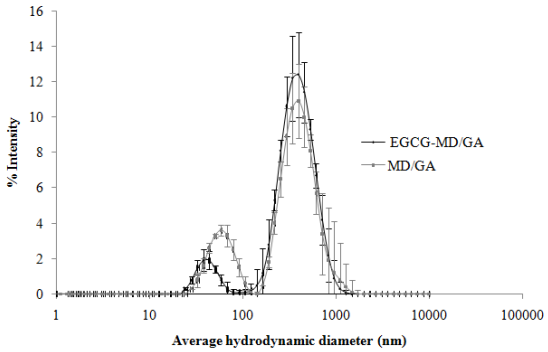

Figure 1. Average hydrodynamic diameter distribution of EGCG-loaded particles and unloaded (MD/GA) nanoparticles.

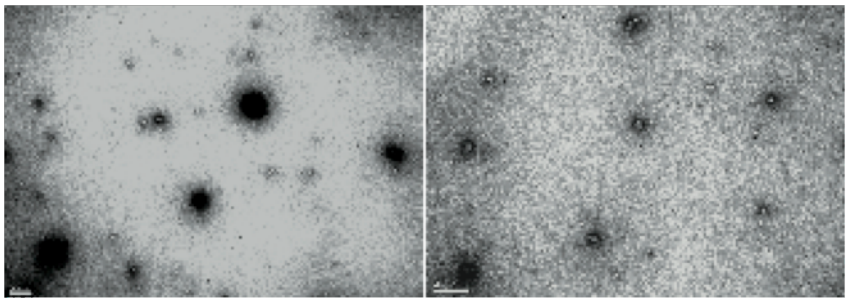

Figure 2. Transmission electron microscopy images of polysaccharide nanoparticles. The scale bar is 200 nm.

Table 1. Relative diffusion coefficients (related to TSP), with calculated standard deviations (in italics) of EGCG and MD/GA in D_2O at 30 °C for the samples studied.

Sample	EGCG (δ, ppm)	MD and GA (δ, ppm)					
	7.03	5.42	5.25	4.1-3.5	3.43	3.3	1.28
EGCG	0.62						
	0.01						
MD/GA		0.40	0.55	0.28	0.37	0.52	0.04
		0.04	*0.01*	*0.03*	*0.02*	*0.02*	*0.03*
EGCG-MD/GA	0.45	0.37	0.52	0.30	0.37	0.50	0.06
	0.03	*0.04*	*0.05*	*0.05*	*0.06*	*0.04*	*0.03*