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Green Synthesis of Multifunctional Nanoparticles from the Plant Polyphenol Quercetin for Drug Delivery

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Despite advances in nanoparticle (NP) therapeutics, there is an unmet need for the scalable synthesis of multifunctional nanocarriers to meet the complex challenges of drug delivery. Here we have synthesized a versatile nanoscale platform from quercetin (QCT) by simple mixing under ambient conditions. NPs (~30-40 nm in diameter) were formed by oxidative self-polymerization of QCT in alkaline buffer (pH 9), in a process mimicking that of mussel-inspired catechol polymerization. The propensity of oxidized polyphenols to react with nucleophiles was exploited to functionalize the NPs with amine-terminated methoxy poly(ethylene glycol) (mPEG-NH_2) to impart steric stability. The NPs were loaded with doxorubicin (DOX) as a model drug, and KB cells were used for *in vitro* bioassays. Surface modification of the NPs with mPEG-NH_2 was confirmed by Dynamic Light Scattering and X-ray Photoelectron Spectroscopy. Cytotoxicity assays showed the NPs to be nontoxic up to 1 mg/mL, while retaining some antioxidant activity. DOX-loaded NPs showed high drug loading efficiency, sustained release, and potent cytotoxicity *in vitro*. Our findings present a promising new application for naturally occurring polyphenols such as QCT as a renewable source of nanocarriers that can be synthesized at low cost and with minimal equipment.

Keywords: Quercetin; Nanoparticles; Drug delivery; Antioxidant.