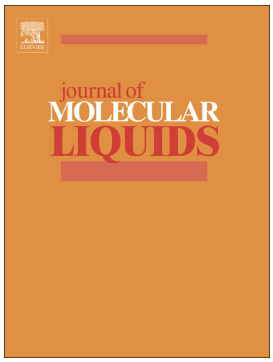

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pH-controlled doxorubicin delivery from PDEAEMA-based nanogels

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((Supplementary Material may be found in the online version of this article.))

ABSTRACT

In this work, the feasibility of some poly(2-(diethylamino)ethyl methacrylate) (PDEAEMA)-based pH-sensitive nanogels as drug nanocarriers is evaluated. The anticancer drug doxorubicin (DOXO) is successfully encapsulated into the nanogels, achieving high drug loading and encapsulation efficiency. It has been found that the *in vitro* delivery of DOXO from the nanogels was pH-dependent: DOXO release rate is accelerated by decreasing pH from 7.4 (healthy cells) to 5.2 (pH condition for endo/lysosomial compartments and unhealthy cells) due to the swelling of the nanogel particles. The uptake of DOXO-loaded nanogels into MDA-MB-231 tumoral cells and the progressive release of the drug from the nanogels to the cell nuclei are demonstrated by fluorescence microscopy measurements. These results suggest a great potential of these DOXO-loaded nanogels for antitumor drug delivery.

KEYWORDS: pH-responsive nanogels, PEGylation, drug delivery systems, doxorubicin, cellular uptake.

INTRODUCTION

Recent advances in the biomedical field have prompted the need to develop delivery systems able to encapsulate therapeutic agents [1-5]. An ideal drug delivery system should target only the -desired cells and tissues and release their cargo at a well-defined time at the intracellular space, responding to specific stimuli such as pH, temperature, and/or redox microenvironments [6]. pH-responsiveness can be exploited for selective drug release at the slightly acidic microenvironment of tumors and/or some cellular compartments (endosomes and lysosomes) [6-8]. Among different pH-sensitive drug delivery systems, cross-linked polymeric nanoparticles, known as nanogels, have found to be specially attractive owing to some potential advantages such as tunable sizes, large surface area, ability to entrap bioactive molecules and also improvement of drug biodistribution and, thereby, therapeutic efficacy [9-11]. Recently, many