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Research Article

MINIMIZING TOXICITY AND IMPROVING CELL UPTAKE OF DIMEGLUMINE GADOPENTETATE USING A NEW NON-TOXIC AND BIOCOMPATIBLE CHITOSAN-CARBON QUANTUM DOT HYBRID NANOGEL IN HEK293 AND MCF7 CELL LINES

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ABSTRACT

Magnetic resonance imaging (MRI) contrast agents have been used routinely for more than 20 years in order to increase sensitivity and specificity of lesion detection. Gadolinium contrast media are chemical substances used in MRI scans. dimeglumine gadopentetate is one of the gadolinium-based MRI contrast agents. Gadolinium based Contrast agents (CAs) show significantly toxicity profiles. Recently, a delayed serious adverse reaction known as nephrogenic systemic fibrosis (NSF) has been reported in patients, with a marked reduction in renal function after administration of gadolinium based CAs. For gadolinium based CAs, the emerging unexpected cytotoxicity has become a new concern. In this research, antitoxic biochemical and molecular potential basis of Chitosan coated on quantum carbon dot loaded on dimeglumine gadopentetate so as to reduce toxicity of dimeglumine gadopentetate was examined. To determine Chitosan loaded on quantum carbon dot AFM, FTIR and DLS were used. Also UV-Visible was used to prove Magnevist loaded on the new nanogel correctly. In order to evaluate the new nanogel- drug toxicity in coparson with the drug MTT was performed on, normal Kidney cell line, HEK-293 cell line. MTT, Flow cytometry and gene regulation assays were done to examine cytotoxic efficiency of new nanogel- drug compared to the drug alone when it exposed to, Brest cancer cell line, MCF7. As well as, cellular uptake of the new nanogel-drug was measured with ICP-Mass and compared with the free dug. Results showed, the new nanogel-drug was able to reduce toxicity of dimeglumine gadopentetate noticeably over HEK-293 cell line (P<0.05). Cytotoxic efficiency of new nanogel-drug showed it was a little more toxic than Magnevist when it exposed to MCF7 cell line. But this effect was negligible when it compared to anticancer drug Chlorambucil.Cellular uptake study was revealed the new nanogel-drug was able to enter cells five times more than Magnevist, however it was a little more in HEK-293 cell line. From our study, the new nanogel composed of quantum carbon dot and chitosan loaded on dimeglumine gadopentetate is a promising thranostic nanogel compared with the contrast agent and potentially suitable for MRI as a new contrast agent.

***KEYWORDS**: Renal failure, Dimeglumine gadopentetate, Quntum carbon dot, Chitosan.*

INTRODUCTION

Contrast Agent is a substance that used as a factor in increasing the amount of contrast in radiation in the field of medical imaging as well as in medical physics. The contrast media used in MRI causes a change in T1 rest time and T2 are different tissues. In addition, making these materials, most efforts are focused on the injection of paramagnetic and ferromagnetic materials. Magnevist is one of the gadolinium-containing compounds used in medical imaging in MRI. Gadopentetate dimeglumine is known as the Magnevist brand [1, 2]. The accumulation and toxicity of gadolinium-based contrast agents: Gadolinium-based contrast agents (GBCAs) after the US Food and Drug Administration authorized gadolinium gadodentinate in 1988 have found widespread use in MRI imaging studies. Different GBCAs are now available for clinical use in one or more regions of the world and it is estimated that more than 200 million doses of this substance are used worldwide [3, 4]. Gadolinium remains important in the body clinically important. Gadolinium is not found naturally in the body. When it enters the tissues of humans and animals, it remains for a long time. In addition, heavy metals are proven to be toxic. As a result, the risk of GBCAs injection into patients with severe renal impairment has been well documented and can lead to Nephrogenic Systemic Fibrosis (NSF) [5]. NSF is a rare, progressive, usually fatal disease characterized by skin thickening, painful joint contractions, and fibroids of multiple organs including the lungs, liver, muscles, and heart. Nearly all documented cases have occurred in patients with chronic severe renal insufficiency who has received gadolinium contrast. The association between gadolinium and NSF was first reported by Danish nephrologists in 2006. Between 2006 and 2010, several hundred cases were diagnosed worldwide .NSF usually develops clinically within days to months following gadolinium exposure, although rare cases have been reported years later. Nearly all patients have been in severe renal failure, and many were on dialysis [6]. Chitosan is a *polysaccharide* amino acid copolymer of 1, 4 D-glucosamine and N-acetyl-glucosamine [7]. Chitosan has a significant potential for tissue regeneration due to biocompatibility, biodegradability and re-absorption and reactivity, and has active amino and hydroxyl groups that can be chemically modified.

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