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Improved anti-tumor activity and reduced cardiotoxicity of Epirubicin using hepatocyte-targeted nanoparticles combined with tocotrienols against hepatocellular carcinoma

N Nafee, M Nasr, H Saad and A Kazem
Alexandria University, Egypt

Hepatocellular carcinoma (HCC) is the third most common cause of cancer death worldwide. Epirubicin (EPI), an anthracycline derivative, is one of the main line treatments for HCC. However, serious side effects including cardiomyopathy and congestive heart failure limit its long term administration. Our main goal is to develop a delivery strategy that ensures improved efficacy of the chemotherapeutic agent together with reduced cardiotoxicity. In this context, EPI was loaded in chitosan-PLGA nanoparticles linked with asialofetuin (EPI-NPs) selectively targeting hepatocytes. In an attempt to reduce cardiotoxicity, targeted EPI-NPs were co-administered with tocotrienols. EPI-NPs significantly enhanced the antiproliferative effect compared to free EPI as studied on Hep G2 cell line. Nanoencapsulated EPI injected in HCC mouse model revealed higher p53-mediated apoptosis and reduced angiogenesis in the tumor. Combined therapy of EPI-NPs with tocotrienols further enhanced apoptosis and reduced VEGF level in a dose dependent manner. Assessment of cardiotoxicity indicated that EPI-NPs diminished the high level of proinflammatory cytokine tumor necrosis factor- α (TNF- α) as well as oxidative stress-induced cardiotoxicity as manifested by reduced level of lipid peroxidation products (TBARS) and nitric oxide (NO). EPI-NPs additionally restored the diminished level of superoxide dismutase (SOD) and reduced glutathione (GSH) in the heart. Interestingly, tocotrienols provided both antitumor activity and higher protection against oxidative stress and inflammation induced by EPI in the heart. This hepatocyte-targeted biodegradable nanoparticle/tocotrienol combined therapy represents intriguing therapeutic strategy for EPI providing not only superior efficacy but also higher safety levels.

Biography

N Nafee is currently working as an Assistant Professor at the Department of Pharmaceutics, Faculty of Pharmacy, Alexandria University, Egypt, where she got her Bachelor and Master degree in Pharmaceutical Sciences. In 2004, she was awarded a 2-year DAAD Doctoral scholarship in the Department of Biopharmaceutics and Pharmaceutical Technology, Saarland University, Germany and completed her PhD degree in 2008, followed by an Alexander von Humboldt Post-doctoral fellowship in the Department of Pharmaceutical Technology and Biopharmacy, Marburg University, Marburg, Germany (2012-2014). She has published 23 research papers in peer-reviewed journals (h-index 10 and >600 citations).

nnafe3@gmail.com

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