World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:14, No:06, 2020

2D and 3D Breast Cancer Cells Behave Differently to the Applied Free Palbociclib or the Palbociclib-Loaded Nanoparticles

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Abstract : Two-dimensional cell culture affords simplicity and low cost, but it has serious limitations; lacking cell-cell and cell-matrix interactions that are present in tissues. Cancer cells grown in 3D culture systems have distinct phenotypes of adhesion, growth, migration, invasion as well as profiles of gene and protein expression. These interactions cause the 3D-cultured cells to acquire morphological and cellular characteristics relevant to in vivo tumors. Palbociclib is a chemotherapeutic agent for the treatment of ER-positive and HER-negative metastatic breast cancer. Poly-amidoamine (PAMAM) dendrimer is a well-defined, special three-dimensional structure and has a multivalent surface and internal cavities that can play an essential role in drug delivery systems. In this study, palbociclib is loaded onto the magnetic PAMAM dendrimer. Hanging droplet method was used in order to form 3D spheroids. The possible toxic effects of both free drug and drug loaded nanoparticles were evaluated in 2D and 3D MCF-7, MD-MB-231 and SKBR-3 breast cancer cell culture models by performing MTT cell viability and Alamar Blue assays. MTT analysis was performed with six different doses from 1000 µg/ml to 25 µg/ml. Drug unloaded PAMAM dendrimer did not demonstrate significant toxicity on all breast cancer cell lines. The results showed that 3D spheroids are clearly less sensitive than 2D cell cultures to free palbociclib. Also, palbociclib loaded PAMAM dendrimers showed more toxic effect than free palbociclib in all cell lines at 2D and 3D cultures. The results suggest that the traditional cell culture method (2D) is insufficient for mimicking the actual tumor tissue. The response of the cancer cells to anticancer drugs is different in the 2D and 3D culture conditions. This study showed that breast cancer cells are more resistant to free palbociclib in 3D cultures than in 2D cultures. However, nanoparticle loaded drugs can be more cytotoxic when compared to free drug.

Keywords : 2D and 3D cell culture, breast cancer, palbociclibe, PAMAM magnetic nanoparticles
Conference Title : ICMBPP 2020 : International Conference on Molecular Biology and Pharmaceutical Biotechnology
Conference Location : Toronto, Canada
Conference Dates : June 18-19, 2020

Open Science Index, Biotechnology and Bioengineering Vol:14, No:06, 2020 publications.waset.org/abstracts/122615/pdf