

European Pharma Congress

August 25-27, 2015 Valencia, Spain

Genotoxicity and cytotoxicity of novel 10B carrier ((2R)-4,5,6-trihydroxy-2-(hydroxymethyl) tetrahydro-2H-pyran-3-yl) boronic acid

Zafer Akan¹, Hulya Ozdemir², Gokhan Oto², Sabahattin Deniz³, Omer Kacar⁴, Ali Sadi Basak⁵, Tahir Cakir⁵, Hatice Uslu Sinav⁶ and Goksel Demir⁷

¹Celal Bayar University School of Medicine, Turkey

²Yuzuncu Yil University, Turkey

³Marmara University, Turkey

⁴TUBITAK Marmara Research Center, Turkey

⁵Yuzuncu Yil University School of Medicine, Turkey

⁶Istanbul Medeniyet University, Turkey

⁷Bahcesehir University School of Engineering, Turkey

Objective: Although surgery and chemotherapy have been greatly successful in the treatment of many types of tumors, these treatment modalities have some limitations. In particular, the side effects of conventional radiotherapy warrant the development of new therapy methods, such as Boron Neutron Capture Therapy (BNCT). In the present study, the cytotoxic and genotoxic properties of novel synthesized boron carrier, ((2R)-4,5,6-trihydroxy-2-(hydroxymethyl)tetrahydro-2H-pyran-3-yl)boronic acid (10BDG), and the apoptotic pathways triggered by 10BDG were examined.

Materials & Methods: As it defined previously, 10BDG was complexed through a low-high pH reaction and was tested using a Fournier Transform InfraRed-Attenuated Total Reflectance (FT-IR/ATR) spectrophotometer. The cytotoxicity of 10BDG was tested through the MTT assay. The detection of caspases 3, 8, and 9 was performed to determine the activated apoptotic pathways by 10BDG. The Poly (ADP-Ribose) Polymerase (PARP) cleavage and DNA damage induced by this compound were tested through western blot and Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay, respectively.

Results: The average LogIC₅₀ and LogLD₅₀ levels of 10BDG over NCI-H209 cell line were to be found 72.1±10 µg/ml and 171.8±25 mg/kg, respectively. Caspase-9 activation, caspase-3 activation, PARP cleavage, and caspase-3-dependent DNA fragmentation were observed. The genotoxicity analysis was performed using the plasmid fragmentation assay, which revealed the absence of fragmentation.

Conclusion: Bio-distribution analysis showed that boron content was elevated to 12.63 from 4.44 ppm in the tumor tissue by the 10BDG injections. In epitome, 10BDG exhibit slight cytotoxic but no genotoxic properties. Based on the antiproliferative properties of 10BDG, in addition to acting as an adjuvant in cancer radiotherapy and chemotherapy, this compound appears to be an alternative boron carrier for BNCT.

hulyaozdemir@yyu.edu.tr

Notes: