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Epoxomicin Affects Proliferating Neural Progenitor Cells of Rat

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Abstract : Developmental neurotoxicity (DNT) entails the toxic effects imparted by various chemicals on the brain during the early childhood period. As human brains are vulnerable during this period, various chemicals would have their maximum effects on brains during early childhood. Some toxicants have been confirmed to induce developmental toxic effects on CNS e.g. lead, however; most of the agents cannot be identified with certainty due the defective nature of predictive toxicology models used. A novel alternative method that can overcome most of the limitations of conventional techniques is the use of 3D neurospheres system. This in-vitro system can recapitulate most of the changes during the period of brain development making it an ideal model for predicting neurotoxic effects. In the present study, we verified the possible DNT of epoxomicin which is a naturally occurring selective proteasome inhibitor with anti-inflammatory activity. Rat neural progenitor cells were isolated from rat embryos (E14) extracted from placental tissue. The cortices were aseptically dissected out from the brains of the fetuses and the tissues were triturated by repeated passage through a fire-polished constricted Pasteur pipette. The dispersed tissues were allowed to settle for 3 min. The supernatant was, then, transferred to a fresh tube and centrifuged at 1,000 g for 5 min. The pellet was placed in Hank's balanced salt solution cultured as free-floating neurospheres in proliferation medium. Two doses of epoxomicin (1µM and 10µM) were used in cultured neuropsheres for a period of 14 days. For proliferation analysis, spheres were cultured in proliferation medium. After 0, 4, 5, 11, and 14 days, sphere size was determined by software analyses. The diameter of each neurosphere was measured and exported to excel file further to statistical analysis. For viability analysis, trypsin-EDTA solution were added to neurospheres for 3 min to dissociate them into single cells suspension, then viability evaluated by the Trypan Blue exclusion test. Epoxomicin was found to affect proliferation and viability of neuropsheres, these effects were positively correlated to doses and progress of time. This study confirms the DNT effects of epoxomicin on 3D neurospheres model. The effects on proliferation suggest possible gross morphologic changes while the decrease in viability propose possible focal lesion on exposure to epoxomicin during early childhood.

Keywords : neural progentor cells, epoxomicin, neurosphere, medical and health sciences
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