Abstract

Preclinical studies have revealed that potassium channel openers (KCOs) showed neuroprotective activity in various in-vitro and in-vivo experiments. However, their effect and mechanism of action in brain stroke related disorders such as diabetes mellitus and Alzheimer’s disease remain poorly understood. Hence present study was conducted to evaluate in-vitro anti-oxidant activity, in-vitro neuroprotective activity in glioblastoma cell line and in-vivo neuroprotective activity of potassium channel openers in ischemic brain stroke related disorders diabetes mellitus and Alzheimer’s disease. To find out mechanism of neuroprotection by potassium channel openers, we induced ischemic type of brain stroke using transient middle cerebral artery occlusion (tMCAO) method in diabetic animals and in animals treated with AlCl₃ to induce Alzheimer’s like dementia. For in-vitro methods, % of DPPH scavenging effect and IC₅₀ values for reducing power and inhibition of lipid peroxidation were calculated. In cell line study, cell viability assay was done for the evaluation of protective effect of KCOs on hydrogen peroxide (H₂O₂) induced neuronal toxicity in glioblastoma cells. Various parameters measured in in-vivo models were serum glucose level, neurological score, infarct volume, physical parameters, serum lipid profile, level of ketone bodies, oxidative stress parameters, caspase-3 level, acetylcholinesterase activity (AchE) and VEGF (vascular endothelial growth factor) level. Result of our study showed that cromakalim, nicorandil and cinnarizine produces in-vitro anti-oxidant activity in terms of DPPH radical scavenging activity, thiobarbituric acid (TBA) assay, reducing power assay and neuroprotective effect against H₂O₂ induced neuronal injury. In-vivo studies showed improvement in neuronal function as well as various biochemical parameters level by pretreatment with cromakalim and nicorandil in streptozotocin induced type-I diabetic ischemic rats (acute type model) and AlCl₃ treated ischemic rats by treatment with KCOs. These effects were consistent with vitamin E.