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(57) Abstract :
In the present study, two structurally diverse novel glitazones were synthesized for activation of central PGC-1a signaling through stimulation of PPARR-y receptor. The functional interaction between PGC-1a and PPAR-y is a key interaction in the normal physiology of neuroprotective mechanism. Therefore, activation of PPAR-y dependent PGC-1a co-activator signalling cloud be an effective strategy to exhibit neuroprotection in several neurodegenerative disorders like Alzheimer's disease, Parkinson's disease, and cerebral ischemia. Analogs were designed manually based on principles of bioisosterism. The designed two glitazones (G1, G2) were synthesized and structurally analysed. As part of evaluation, synthesized glitazones were subjected for preliminary neuroprotective evaluation in lipopolysaccharide (LPS) intoxicated SH-SY5Y neuroblastoma cells. The results indicate that pre-treatment with synthesized glitazones have increased the percentage cell viability, protected the cell morphology and decreased the release of pro-inflammatory cytokines (IL-1ß, TNF-a), lipid peroxide (LPO), and nitric oxide (NO) level in LPS intoxicated SH-SY5Y cells. Interestingly, among the two glitazones, G2 has shown significant neuroprotection in comparison to G1 and neuroprotective effect