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(57) Abstract :
The present invention provides a composition comprising an amount of glitazone derivatives effective to provide neural protection under neuroinflammatory circumstances in the brain cells. The glitazone derivatives compounds as new PPAR-gamma agonists are designed and analyzed using in-silico computational approaches for their binding affinity to activate PGC-1alpha via PPAR-gamma binding. The potential glitazone compounds are (E)-2-(4-oxo-5-(4-(2-oxo-2-(thiazol-2-ylamino)ethoxy)benzylidene)-2-thioxothiazolidin-3-yl)acetic acid; (E)-2-(5-(4-(2-((4-chlorophenyl)amino)-2-oxoethoxy)benzylidene)-4-oxo-2-thioxothiazolidin-3-yl)acetic acid; and (E)-2-(5-(3-methoxy-4-(2-oxo-2-(pyridin-2-ylamino)ethoxy)benzylidene)-4-oxo-2-thioxothiazolidin-3-yl)acetic acid. The In-vitro cytotoxicity study using MTT assay in SH-SY5Y human neuroblastoma cells performed by five different doses of glitazone derivatives are 6.25, 12.5, 25, 50 and 100µM/ml and In vitro cytotoxicity study of SH-SY5Y human neuroblastoma cells show potential compounds have IC50 values of 59.64µM, 78.56µM and 43.22µM. The concentration of the potential compounds for assessing membrane potential of mitochondria in SH-SY5Y cell line is 16µG/mL. The %SHSY5Y cells expressed IL-6, TNF-alpha and NF-kB cytokines in Lipopolysaccharide+PP001 are 2.64%, 18.6% and 24.41% respectively. The assay indicates that compounds showed activation of PGC-1alpha signaling via good binding affinity for PPAR-gamma in Lipopolysaccharide induced SHSY5Y cells. The PPAR-gamma protein binding affinity (TRFRET assay) of compounds PP001, PP002, PP010 show IC50 are 4.62, 3.50, 2.92 and 1.77µM, respectively. The composition of glitazone derivatives may provide neural protection under cytotoxic and neuroinflammatory circumstances in the brain cells.

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