Title: *In Silico* modelling and *in vitro* characterization to develop a novel drug which can inhibit one of the principal protein translation machineries, m7G-eIF4E - An innovative approach.

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Background: Protein translation is one of the fundamental, basic and intricate machinery process in the biology of the cell. Deregulation of protein translation has serious implication in cellular health and might contribute to progression of cancer and neurodegenerative disorders such as Parkinson's Disease. To take it under control we found a novel strategy by disrupting m7G-eIF4E interaction.

Methods:
In Silico Approach: Computational simulation, Ligand preparation, Ligand docking, Molecular Dynamics simulation by using Schrodinger.
In Vitro Approach: MTT Assay to get IC_{50} of Diosmin on SHSY5Y neuroblastoma cell line, Western Blot to check the global protein synthesis, Immunocytochemistry to check the apoptosis, chromatin condensation, cell proliferation and DNA repairment capability.

Results: Our computational studies reveal that Diosmin interacts with critical amino acid residues involved in inhibition of eIF4E (Trp56 and Trp102) with acceptable Protein and Ligand fluctuations of 1.2Å and 0.1Å respectively. SUnSET assay confirms that 25μM Diosmin decreased the global protein synthesis rate at 70%. 25μM Diosmin induced 8% of apoptosis and 19% of chromatin condensation compares to control. Also, Diosmin doesn't cause the reduction of cell proliferation and DNA repairment significantly at 25μM concentration but at higher concentrations.

Discussion and Conclusion: Increase protein translation leads to Parkinson's disease (PD) induced by pathologic a syn through mTOR dependent pathway. Recent research has shown that inhibition of S6K, a crucial protein translation machinery prevents the dopaminergic neuron loss. So, we have found out a novel approach to inhibit the protein translation by disrupting m7G-eIF4E in PD biology. Diosmin, a m7G cap competitor has successfully inhibited the protein translation at 25μM conc. while causing a minimal amount of cell death and usual rate of cell proliferation.

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