Title:	Epigenetic regulation mediated nanotheraphy for inhibition of Parkinson's disease
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Abstract:	Parkinson's disease (PD) is the second most common progressive neurodegenerative infirmity. The recent pharmacological and innovative surgical approaches are effective but have multiple side effects. Therefore, it is imperative to introduce new anti-PD agents. In this regard, the present thesis enlightens the nanotherapeutic applications and underlying neuroprotective mechanisms by overcoming the existing limitations of promising neurotherapeutic agents including metformin, Hytrin, and FTY720. The nature-inspired polydopamine nanoparticles, polydopamine-serotonin nanohybrids, chitosan nanoparticles, and FTY720 nanoparticles have shown endowment in the therapeutic efficacy of metformin, Hytrin, and FTY720 in vitro, ex vivo,and in vivo experimental PD models, respectively. The presented biocompatible nanostructures exhibited brain retention, anti-inflammatory activity, and a slower drug release profile leading to neuroprotection against PD deficits. The known molecular therapeutic target of PD, alpha-synuclein has been focused on the exploration of epigenetic regulation to understand the neuroprotective mechanisms of presented nanocomposites. The thesis has predominantly explored epigenetic regulation in the nanotherapeutic intervention of PD by understanding the camouflaged role of EZH2, the epigenetic master regulator, and targeting H3K27ac in the reduction of synucleinopathy to retard PD. Cumulatively, the nanostructures have shown EZH2- mediated endowment in ubiquitination/proteasomal degradation of phosphorylated alpha-synuclein. The non- canonical role of PP2A was also revealed in the EZH2-mediated degradation of phosphorylated alpha-synuclein. The thesis also emphasized and explored the nanocomposites-mediated deacetylation of H3K27ac to halt synuclein gene (SNCA) expression in PD retardation. Thus, the thesis divulges nature-inspired nanocomposites- mediated neuroprotective actions by highlighting epigenetic regulation in PD treatment as an emerging and promising therapeutic target. The thesis has presented work has the promising significance due to utilization of widely known biocompatible and utrastable nanocarriers with already FDA approved drugs. Hence, repurposing of these FDA approved drugs with presented nanoformulations may lead to provide breakthrough in PD treatment if they will further investigated in the clinical setup. The major limitation of presented work is that the long-term toxicity and chronic dose toxicity of nanoformulation has not investigated with comparison of commercially available PD drugs.
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