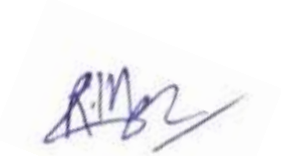
Summary of the research work

Therapeutic options for Parkinson Disease (PD) are limited to a symptomatic approach making it a global threat. Targeting aggregated alpha-synuclein (α-syn) clearance is a gold standard for ameliorating PD pathology bringing autophagy into the limelight. Expression of autophagy related genes are under the regulation by histone modifications, however, its relevance in PD is yet to be established. Here, preformed fibrillar form (PFF) of α-syn was used to induce PD in wistar rats, which were thereafter subjected to treatment with trehalose (tre, 4g/kg, orally), a potent autophagy inducer and sodium butyrate (SB, 300mg/kg, orally), a pan histone deacetylase inhibitor alone as well as in combination. Combination treatment significantly reduced motor deficits as evidenced after rotarod, narrow beam walk and open field test. Novel object location and recognition test was performed to govern cognitive abnormality associated with advanced stage PD which was overcome by the combination treatment. Additionally, level of pro-inflammatory cytokines significantly reduced, along with elevated level of dopamine and histone H3 acetylation was found after treatment with the combination. Further, mRNA analysis revealed that levels of certain autophagy related genes and proteins implicated in PD pathogenesis significantly improved after administration of both tre and SB. Immunofluorescence and H&E staining in the substantia nigra region mirrored potential improvement after treatment with both tre and SB. Therefore, outcomes of the present study were adequate to prove that combinatorial efficacy with tre and SB may be a formidable insight to ameliorate PD exacerbated by PFF α-syn as compared to its individual efficacy.



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