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Dysregulation of autophagy has been involved in a wide range of environmental chemical-induced neurotoxicity [61]. Moreover, strong evidence indicates that dysfunctional autophagy leads to the aggregation of abnormal proteins, including α -synuclein [62], or accumulation of damaged cell organelles in models of PD [63]. Impairment of autophagy have been demonstrated in patients with Lewy body disease and in a model of α -synucleinopathy. It has been reported that α -syn can interfere with the early stages of autophagosome formation. Thus, the accumulation of α -syn is cytotoxic for the neurons and can also cause a disruption of the autophagy process, leading to even faster accumulation of proteins [64]. The present study employed the ROT as an environmental chemical neurotoxin and is capable of induction of PD in rats [65].

LC3 is extensively recognized as an autophagic indicator to assess the activity of autophagy as it is is present in the membrane of the autophagosome [66]. In addition, P62 is an autophagy receptor that interacts with ubiquitinated cargo and LC3 [67] and is considered a hallmark of autophagic flux, during which P62 is constantly degraded [68]. Thus, high LC3/low P62 suggests activated and intact autophagy, while low LC3/p62 may show low basal autophagy [69].

Here, we demonstrated downregulation of LC3 gene and protein expressions, along with an increased P62 level in the midbrain of ROT-treated rats signifying a suppressive effect of ROT on autophagy pathways. Our results were in accordance with the previous finding showing that ROT administration resulted in a decreased LC3 and Beclin-1 expression, and an increased P62 protein level [70].

Recent reports demonstrated that vitamin D supplementation elevates the basal levels of autophagy and lowers oxidative stress parameters [71]. Serum levels of vitD in PD patients have been found to be approximately two times lower than in healthy subjects, suggesting that there may be a correlation between the vitD level and autophagy in PD [72]. Interestingly, vitamin D modulates autophagy at several levels throughout different mechanisms, including the regulation of intracellular calcium levels and its downstream pathways [73]. Tavera-Mendoza et al. reported that the vit D receptor (VDR) acts as





