Inhibition of the Parkinson's disease-related protein DJ-1 by endogenous neurotoxins of the 1,2,3,4-tetraisoquinoline family

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Abbreviations: ADTIQ, 1-acetyl-6,7-dihydroxy-1,2,3,4-tetrahydroquinoline; AGEs, advanced glycation end products; aSyn, alpha-synuclein; BSA, bovine serum albumin; Cat, catalase; DTT, dithiothreitol; GDP, guanosine diphosphate; IsoADTIQ, regioisomer of ADTIQ; MGO, methylglyoxal; PBS, Phosphate Buffer Saline; PD, Parkinson's disease; pNPA, para-nitrophenyl acetate; ROS, reactive oxygen species; SOD, superoxide dismutase; ThT, Thioflavin T; TIQs, 1,2,3,4-tetraisoquinoline family.

Figure S1. Esterase activity of DJ-1 towards pNPA as substrate.

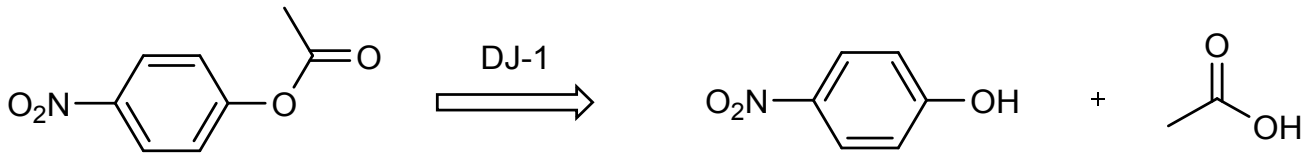

Figure S2. Protective activity of DJ-1 against glycation of GDP by MGO.

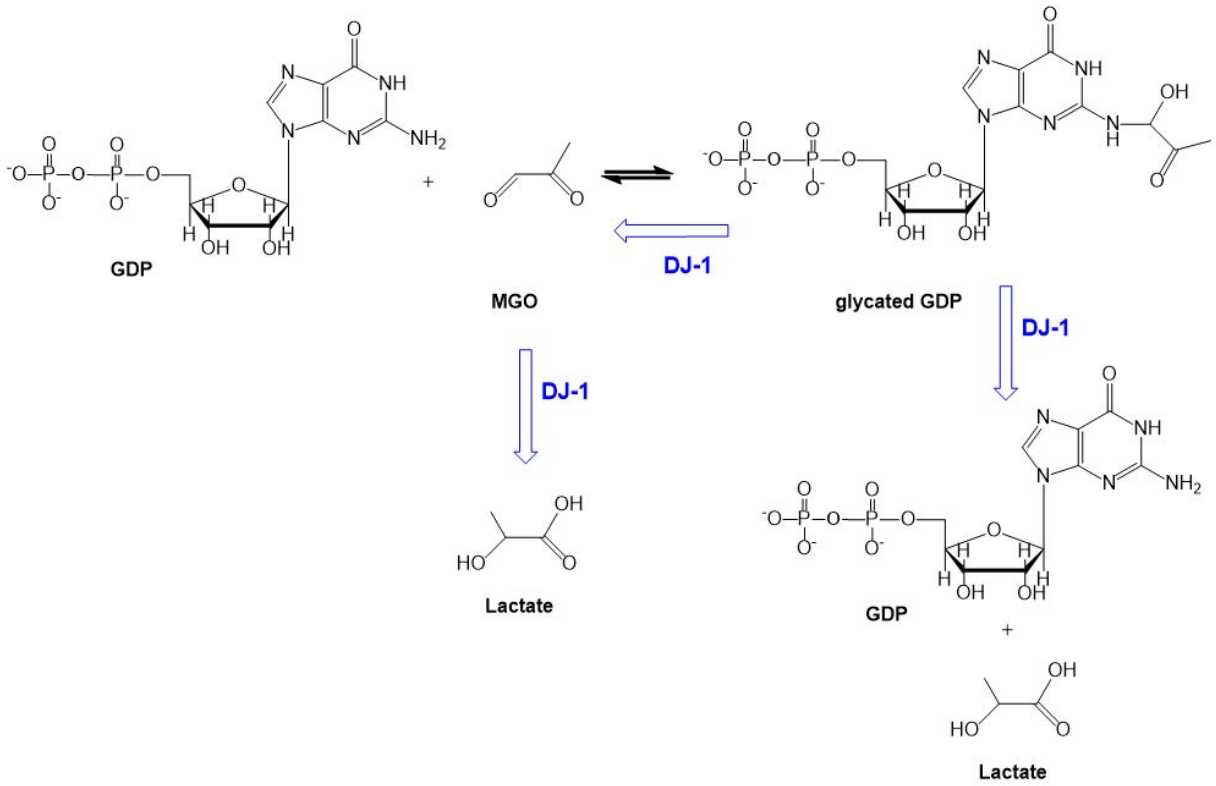

Figure S3. Inhibition of the DJ-1 esterase activity with ADTIQ before and after dialysis. *The DJ-1 (1 µM final) was first incubated in presence or absence of ADTIQ (100 µM) for 30 min at 37°C. The samples were then dialyzed overnight at 4°C against phosphate buffer prior to enzyme assay. Controls were carried out with non-dialyzed samples.*

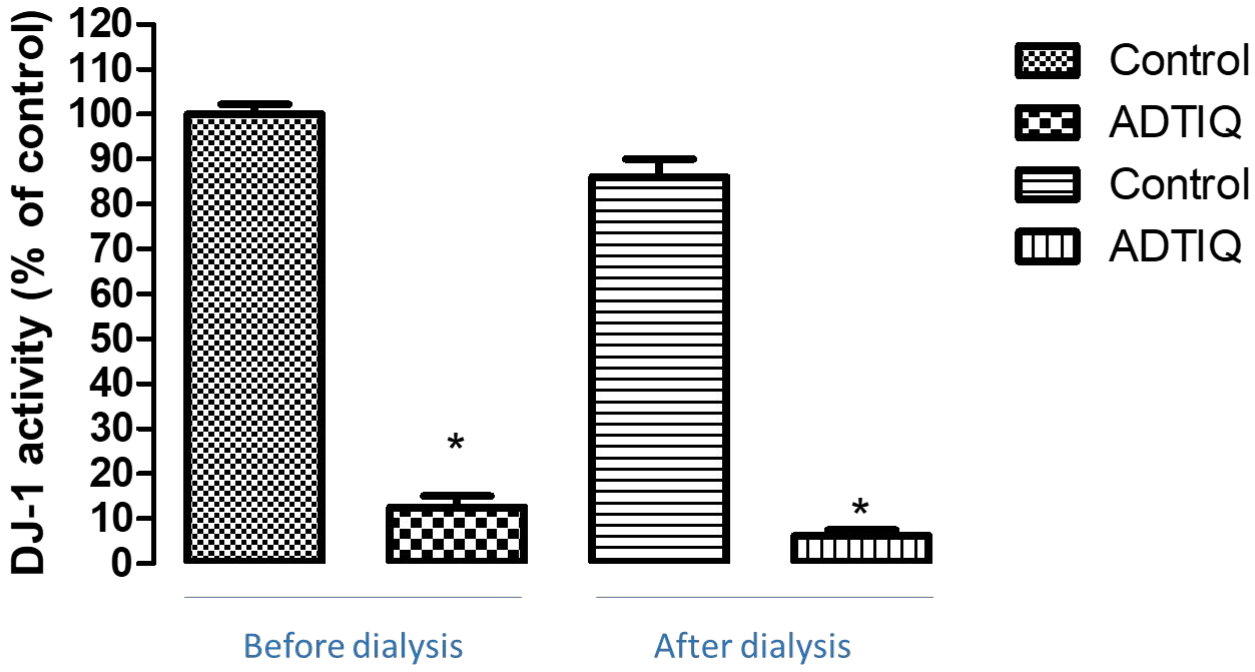

Figure S4. Fibrillization kinetics of aSyn. *The ThT assay was conducted in phosphate-buffered saline (PBS) at pH 7.4. The final concentrations of aSyn, ThT, MGO, DJ-1, and ADTIQ were 50 μM, 25 μM, 1 mM, 10 μM, and 100 μM, respectively. The signal was normalized to the plateau signal of the aSyn condition.*

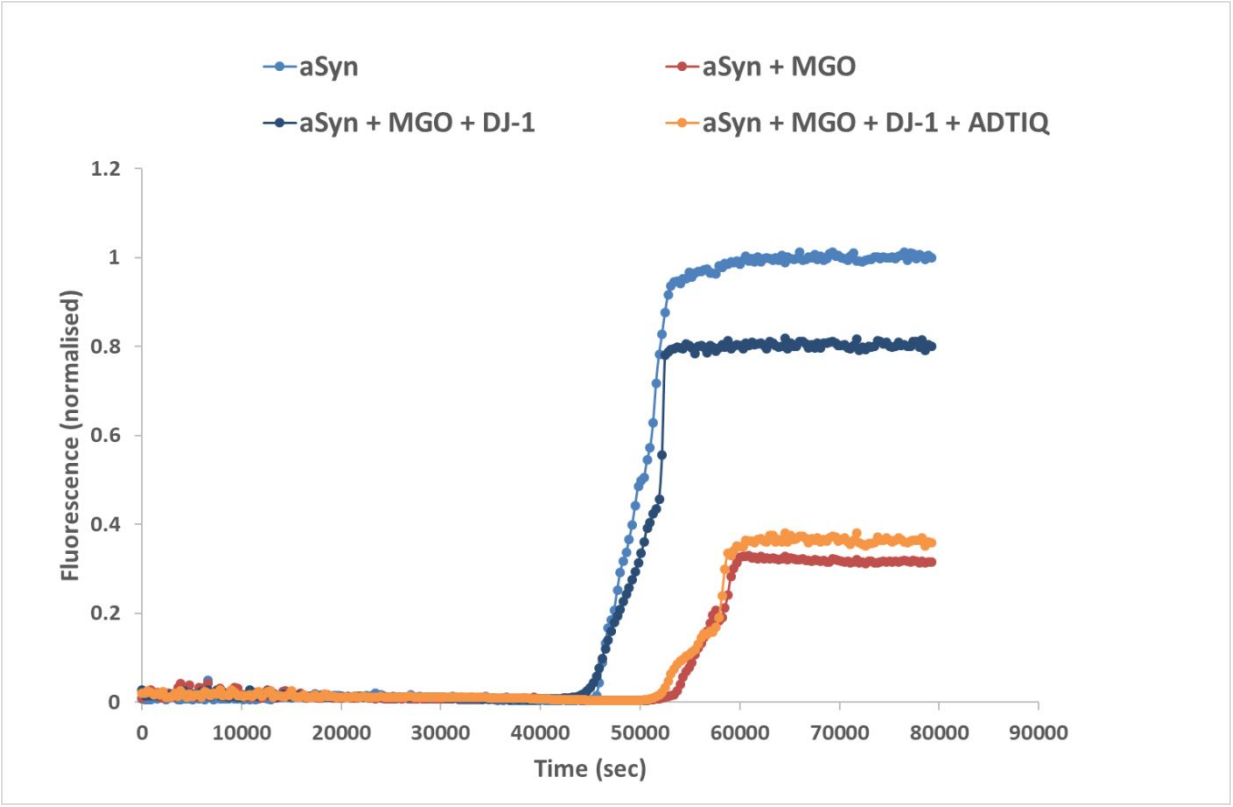

Figure S5. The roles of SOD/Cat in the protection of CYS106 oxidation by TIQs.

A: Dotblot analysis of the oxDJ-1 (using an antibody against CYS106 oxidized DJ1) under the following conditions:
Upper line - 1. DJ-1 (2 µg), 2. DJ-1 (2 µg) incubated 1h with ADTIQ (100 µM), 2. DJ-1 (2 µg) incubated 1h with isoADTIQ (100 µM), 4. DJ-1 (2 µg) incubated 1h with H_2O_2 (100 µM).
Bottom line - 1. DJ-1 (2 µg) incubated 1h with SOD/Cat, 2. DJ-1 (2 µg) incubated 1h with SOD/Cat and ADTIQ (100 µM), 2. DJ-1 (2 µg) incubated 1h with SOD/Cat and isoADTIQ (100 µM), 4. DJ-1 (2 µg) incubated 1h with SOD/Cat and H_2O_2 (100 µM).

B: Inhibition of the esterase activity of DJ-1 by TIQs and prevention by SOD/Cat mixture