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Trigonelline, a jellyfish alkaloid, in the restoration of cathepsin B and D activity in the substantia nigra and caudate putamen in a rat model of Parkinson's disease

Alquiandra S.F. Mançano[1], Juliana Pina[1], Ana Carolina P. Campos[2], Rosana L. Pagano[2], Bianca Zychar[3], Juliana Mozer Sciani[1]

[1] Laboratory of Natural Products, Universidade São Francisco, Bragança Paulista, CEP: 12916-900, Brasil

[2] Laboratory of Neuroscience, Hospital Sírio-Libanês, São Paulo, CEP 01308-050, Brasil

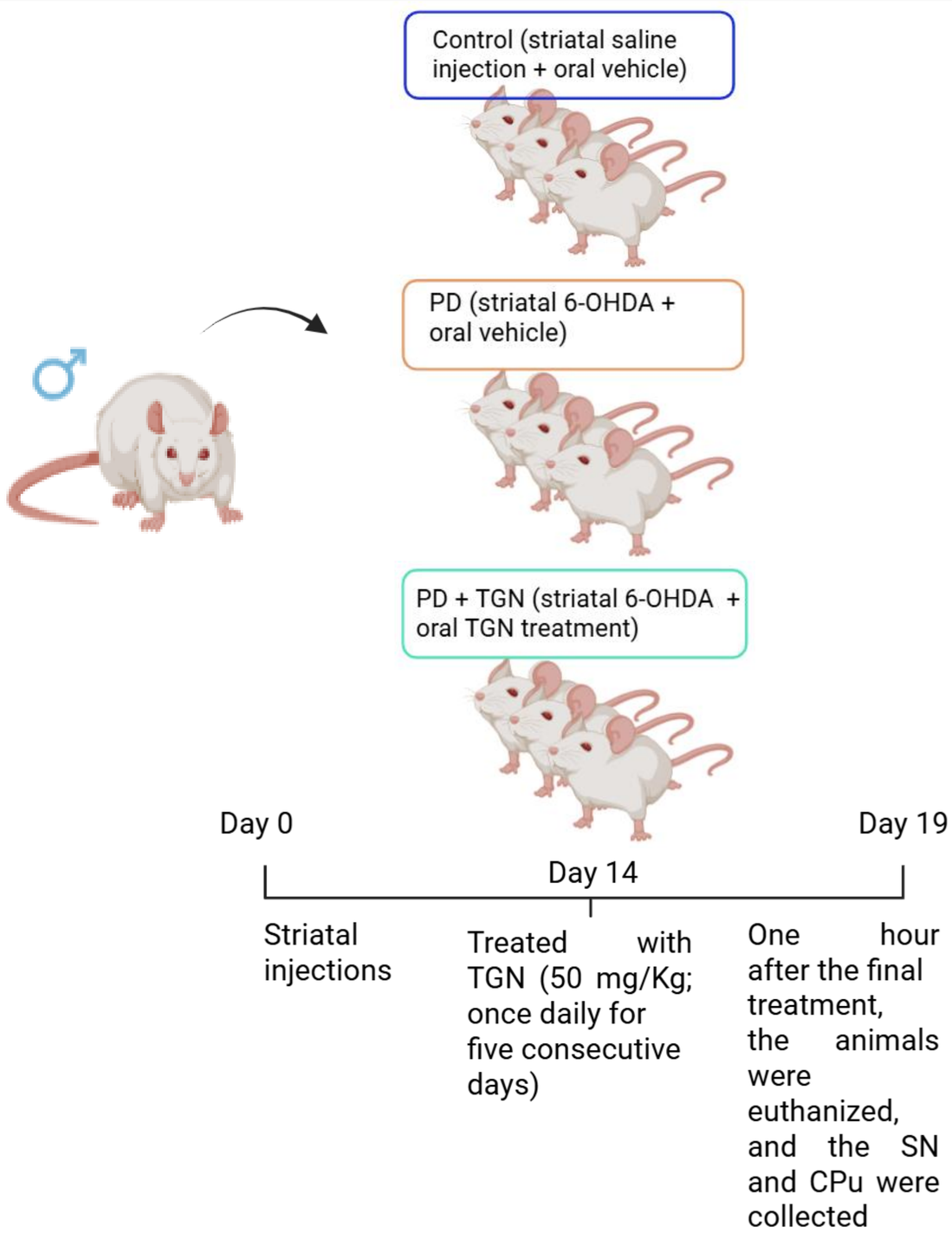
[3] Laboratory of Physiopathology, Instituto Butantan, São Paulo, CEP: 05503-900, Brasil

alquiandra.mancano@mail.usf.edu.br

INTRODUCTION

Parkinson's disease (PD) is characterized by the progressive degeneration of dopaminergic neurons in the nigrostriatal pathway, primarily due to misfolded α-synuclein. Lysosomes play a crucial role in degrading these proteins through cathepsins, a mechanism impaired in PD. Trigonelline (TGN), an alkaloid found in plants and identified in jellyfish by our research group, has been shown to inhibit caspase-1. Its analog, nicotinic acid, has demonstrated beneficial effects in PD models. This study investigates the modulation of cathepsin D (CTSD) and cathepsin B (CTSB) activity by TGN in the substantia nigra (SN) and caudate putamen (CPu) of PD-induced rats.

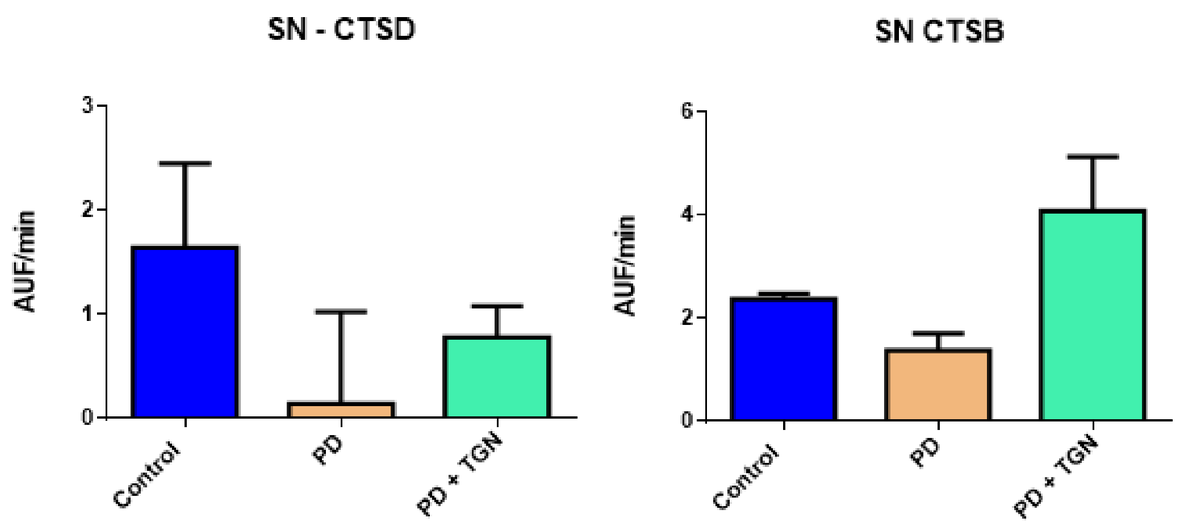
METHOD



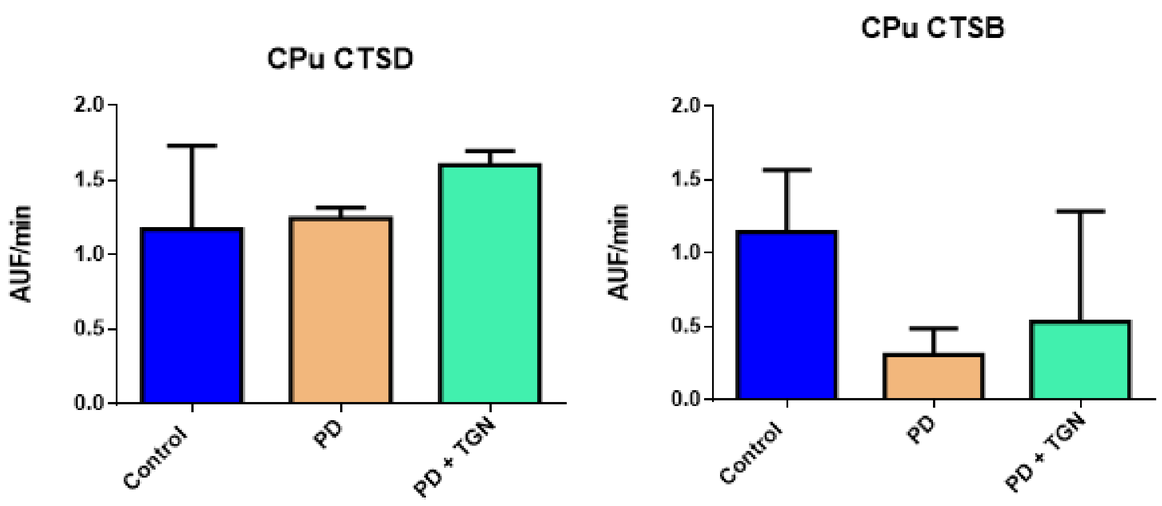
For enzymatic activity analysis using specific substrates. Fluorescence was measured every five minutes over 50 minutes.

RESULTS & DISCUSSION

Preliminary findings indicate that in the PD model, CTSD activity in the right SN was reduced (Control = 1.65 AUF/min; PD = 0.14 AUF/min), as was CTSB activity (Control = 2.37 AUF/min; PD = 1.37 AUF/min). TGN treatment enhanced the activity of both enzymes (CTSD = 0.79 AUF/min; CTSB = 3.07 AUF/min).



In the CPu, CTSD activity remained similar among groups, whereas CTSB activity was reduced in PD but was not restored by TGN



CONCLUSION

TGN enhances the activity of key lysosomal enzymes in the SN, which is associated with removing protein aggregates. These findings suggest a potential role for TGN in maintaining lysosomal functionality in this critical brain region affected by PD.

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