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Schisandra chinensis protects against dopaminergic neuronal oxidative stress, neuroinflammation and apoptosis *via* the BDNF/Nrf2/NF-κB pathway in 6-OHDA-induced Parkinson's disease mice

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by a disorder of both the motor and nonmotor systems due to a loss of dopaminergic (DA) neurons. Herein, we aimed to investigate the potential neuroprotective role of Schisandra chinensis (Sch) and to determine the mechanism by which Sch functions to ameliorate PD in a 6-hydroxydopamin (6-OHDA)-induced PD model. The open field test, sucrose preference test, and Y-maze test were utilized to evaluate the motor and nonmotor symptoms. We found that administration of Sch improved both disorders and DA neurodegeneration in 6-OHDA-induced mice. Additional data confirmed that Sch treatment significantly increased BDNF expression and decreased the activity of GSK-3β in the striatum and hippocampus. Moreover, Sch was able to alleviate the abnormal levels of ROS and increase SOD by boosting Nrf2 expression. The nuclear translocation of NF-κB was inhibited by Sch, which subsequently led to a downregulation of proinflammatory cytokines. Sch effectively suppressed apoptosis by decreasing expressions of caspase 3, caspase 9, and p53 in the PD mouse model. Our findings demonstrate that Sch protects against DA neurodegeneration in 6-OHDA-induced PD mice by suppressing oxidative stress, neuroinflammation and apoptosis through the involvement of the BDNF/Nrf2/NF-κB signaling pathway.

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Introduction

Parkinson's Disease (PD) is the second most common degenerative disease of the central nervous system. It is a neurological disorder with evolving layers of complexity and is associated with dopaminergic (DA) neuron deficiency and both motor and nonmotor deficits.[1] PD patients classically develop resting tremor, rigidity, bradykinesia, and stooping posture. PD is also associated with neurobehavioral disorders (*i.e.* depression and anxiety) and cognitive impairment (*i.e.* dementia).[2] PD affects approximately 0.3% of the general population, as well as 1–3% of the population over the age of 65. The number of patients with PD is expected to rise from 8.7 to 9.3 million by 2030.[3] The general accepted incidence of PD ranges from 100 to 200 per 100 000 people, with the annual incidence being 15 per 100 000.[4] However, in the majority of cases, the cause of PD remains unknown.

PD is a multisystemic synucleinopathy that is caused by poorly characterized genetic and environmental factors which cause degeneration of selectively vulnerable neuronal populations. The main pathologic feature that correlates with signs and symptoms of PD is loss of DA neurons and depletion of DA neurons of the striatum,[5] which leads to the development of classical motor symptoms. Recently, more detailed research in this area indicates that the classical view can be extended to other nonmotor-related deficits. Previous literature has reported evidence of oxidative stress in the brain tissues of both familial and sporadic PD patients. Furthermore, oxidative stress is thought to trigger mutations that make cells more vulnerable to dysfunction.[6] Moreover, PD patients are known to have significantly high levels of proinflammatory cytokines in the substantia nigra and cerebrospinal fluid.[7] This immune activation may be caused by, rather than be a response to, the observed DA neuronal loss. Further, techniques such as nuclear TUNEL labeling and chromatin condensation of DA neurons derived from PD brains suggest that these neurons

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