

DOCTORAL THESIS

Pharmacological study of tianma gouteng yin: a traditional Chinese medicine formula for Parkinson's disease

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ABSTRACT

Parkinson's disease (PD) is the second most common neurodegenerative disease affecting 2% of the population over 65 years old that lacks effective cure. The current available treatments for PD are largely symptomatic and palliative. Tianma Gouteng Yin (TGY) is a traditional Chinese medicine (TCM) formula belongs to the formulas that dispel wind. Nowadays, it has been a commonly prescribed formula to treat Parkinsonian-like symptoms such as tremor and paralysis in some of the patients. However, just as most of the TCM formula, the material basis and the underlying pharmacological effects of TGY are still lacking experimental evidence.

In this study, a method using UHPLC/Q-TOF-MS and HPLC-ELSD has been developed and successfully applied to qualitatively and quantitatively determine the complex phytochemicals of TGY. Totally 28 phytochemicals were identified, of which 20 were simultaneously quantified. The material basis profile of TGY decoction was delineated for the first time.

After full component analysis of TGY, the neuroprotective activity of TGY was verified both *in vivo* and *in vitro*. In *Drosophila* PD models, TGY mitigated rotenone induced toxicity and promoted α -synuclein clearance. In stereotaxic rotenone intoxication rats, TGY exerted neuroprotective effects in terms of preventing dopaminergic neurons loss and alleviating neuroinflammation. TGY alleviated rotenone induced apoptosis in SH-SY5Y cells. Furthermore, we discovered that Geniposide, an important component of TGY, is an autophagy inducer both *in vivo* and *in vitro* and is neuroprotective in

transgenic *Drosophila* PD model. In general, our study proves that TGY is neuroprotective in PD models.

In addition to the efficacy study, safety of TGY application in terms of TGY-drug interaction was also evaluated. In our study, herb-drug interactions between TGY and one of the most popular drugs used in PD treatment, Sinemet, were studied. The pharmacokinetics data showed that co-administration of TGY could suppress the absorption of Levodopa, the main component of Sinemet, for the first time. This information suggest that in clinical practice, TGY should avoid been administrated with Levodopa containing medicaments at the same time.

In conclusion, the data of this study provides valuable information on the material basis, efficacy and safety of TGY. This information is useful reference for the clinical application of TGY in PD treatment.

Keywords: Tianma Gouteng Yin, Parkinson's disease, *Drosophila*, Rotenone, α -synuclein, Geniposide, Autophagy, Sinemet, Herb-drug interaction

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