Evaluating the Efficacy of Water-Soluble Ashwagandha and Ubisol-Q10 as Treatment for Mechanisms Implicated in Parkinson's Disease

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Introduction

Parkinson's Disease (PD)

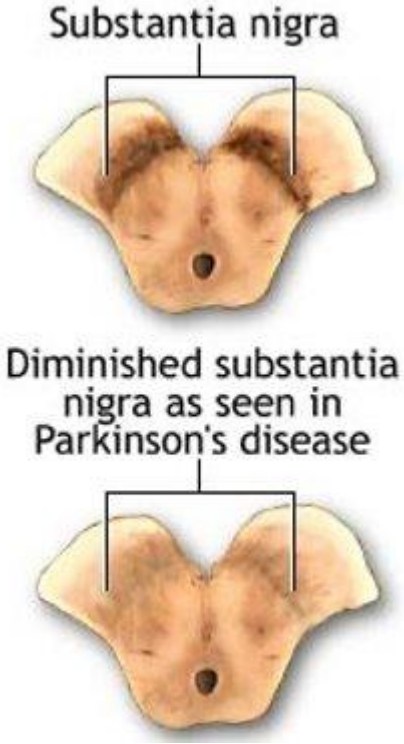
- Common neurodegenerative disorder affecting 2% of the population over 60
- Characterized by a loss of dopaminergic neurons in the substantia nigra, increases in Lewy bodies (α-synuclein aggregates)
- Results in a variety of motor control issues
- Specific cause is unknown, likely genetic and environmental factors

Pathologies:

- Mitochondrial and autophagic dysfunction
- Oxidative stress
- Neuroinflammation

Physical symptoms:

- Tremors
- Balance issues
- Slow movements
- Muscle rigidity



Current Treatments

Levodopa (L-DOPA)

- ➔ Improves dopamine levels
- ➔ Initially alleviates symptoms such as Bradykinesia (slowed-movements)
- ➔ Long-term usage causes permanent motor deficits

Natural Health Products (NHPs)

- ➔ Found to possess neuroprotective properties to alleviate symptoms and prevent progression
- ➔ May avoid negative side effects associated with current treatments
    - ○ Ubisol-Q10
    - ○ Ashwagandha Root Extract

Ubisol-Q10

- ➔ Water-soluble formulation of Coenzyme-Q10 made using polyoxyethanyl-α-tocopheryl sebacate (PTS)
- ➔ Increased bioavailability
- ➔ Reduced dosages to achieve neuroprotection

Previous research with Ubisol-Q10 show:

- ➔ Antioxidant and anti-inflammatory properties
- ➔ Activator of astroglia and autophagy
- ➔ Prevents against senescence and mitochondrial dysfunction

Ashwagandha Root Extract (*Withania Somnifera*)

- ➔ Used in traditional Indian medicine
- ➔ Naturally lipophilic
- ➔ Water soluble formulation was created similar to Ubisol-Q10

Thought to possess many neuroprotective properties:

- ➔ Improved mitochondrial function
- ➔ Anti-inflammatory properties
- ➔ Increased dendrite formation

Research Question and Objectives

Research Question

Can the combination of water-soluble Ashwagandha root extract and Ubisol-Q10 exhibit neuroprotective properties when used as treatment for Parkinson's Disease?

Objectives

1. To compare the neuroprotective properties of water-soluble Ashwagandha and Ubisol-Q10 with treatment and control groups.
2. To evaluate the preservation of dopaminergic neurons in the substantia nigra after treatment with water-soluble Ashwagandha and Ubisol-Q10 through the use of fluorescent staining techniques and the tyrosine hydroxylase antibody.
3. To study the effects of the NHPs on the mechanisms implicated by the progression of the disease including autophagy, oxidative stress, senescence, and inflammation.
4. To analyze the impact of the water-soluble Ashwagandha and Ubisol-Q10 treatment on the expression of pro-survival neurotrophic factors by immunofluorescent staining of the antibodies BDNF, GDNF, and GFAP.

Methods

Rat Model Preparation

5 Treatment groups:

- ➔ Saline + Water control
- ➔ PQ + PTS control
- ➔ PQ + Water-Soluble Ashwagandha Root Extract
- ➔ PQ + Ubisol-Q10
- ➔ PQ + Tonic (Combination treatment of WS-Ashwagandha + Ubisol-Q10)

Paraquat (PQ) Injections

- ➔ Used to induce PD in rat models
  - ◆ 5 injections of 10 mg/kg body weight
  - ◆ 1 injection every 5 days for 25 days

Behavioural Testing + Sacrifice

Preservation of Brain Tissue

- ➔ Whole animal perfusion fixation technique

Methods

Brain Tissue Sectioning + Slide Preparation

Cryoprotection of Brain:
- ➔ 30% sucrose solution submersion

Embedding Matrix + Vacuum Chamber
- ➔ Cerebellum and brainstem removed

Tissue Mounting:
- ➔ Matrix

Tissue Sectioning:
- ➔ Cryostat
- ➔ 30µm at substantia nigra

3 sections/slide

Methods

Stereological Analysis + Immunofluorescent Staining

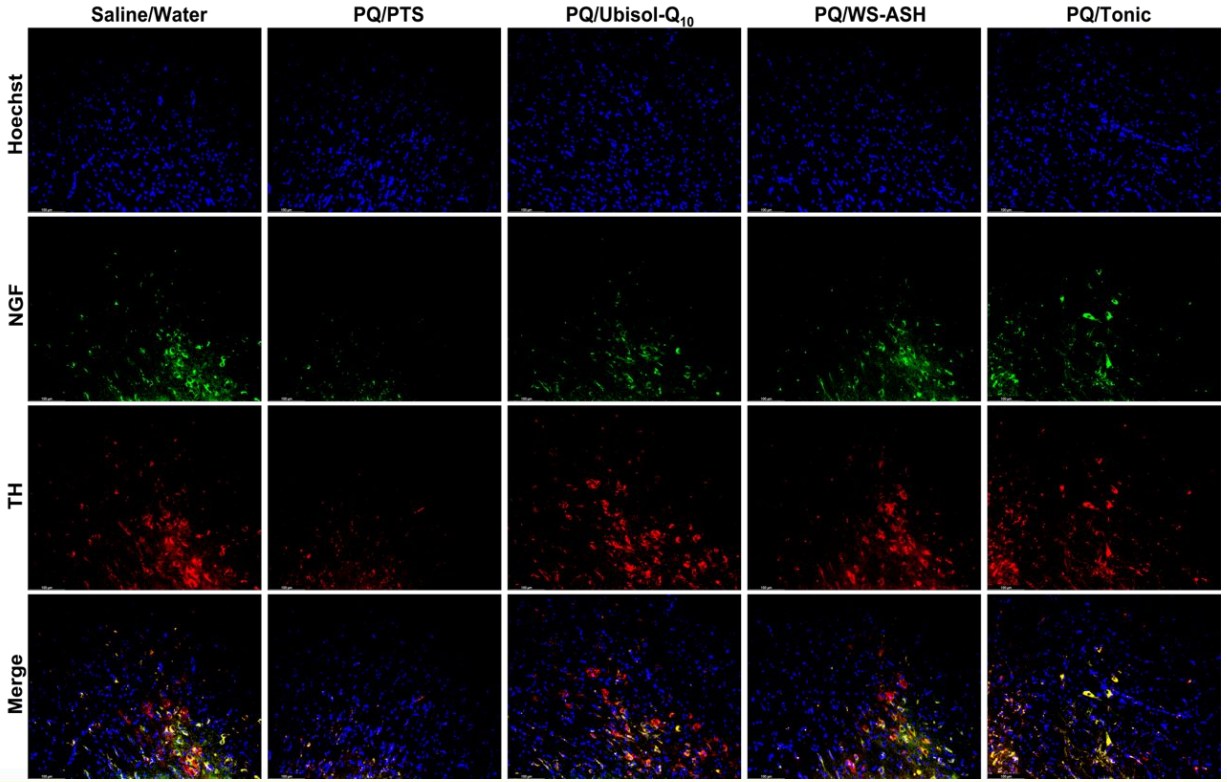
Immunofluorescent Staining and Microscopic Imaging

- ➔ Staining with primary and secondary antibodies

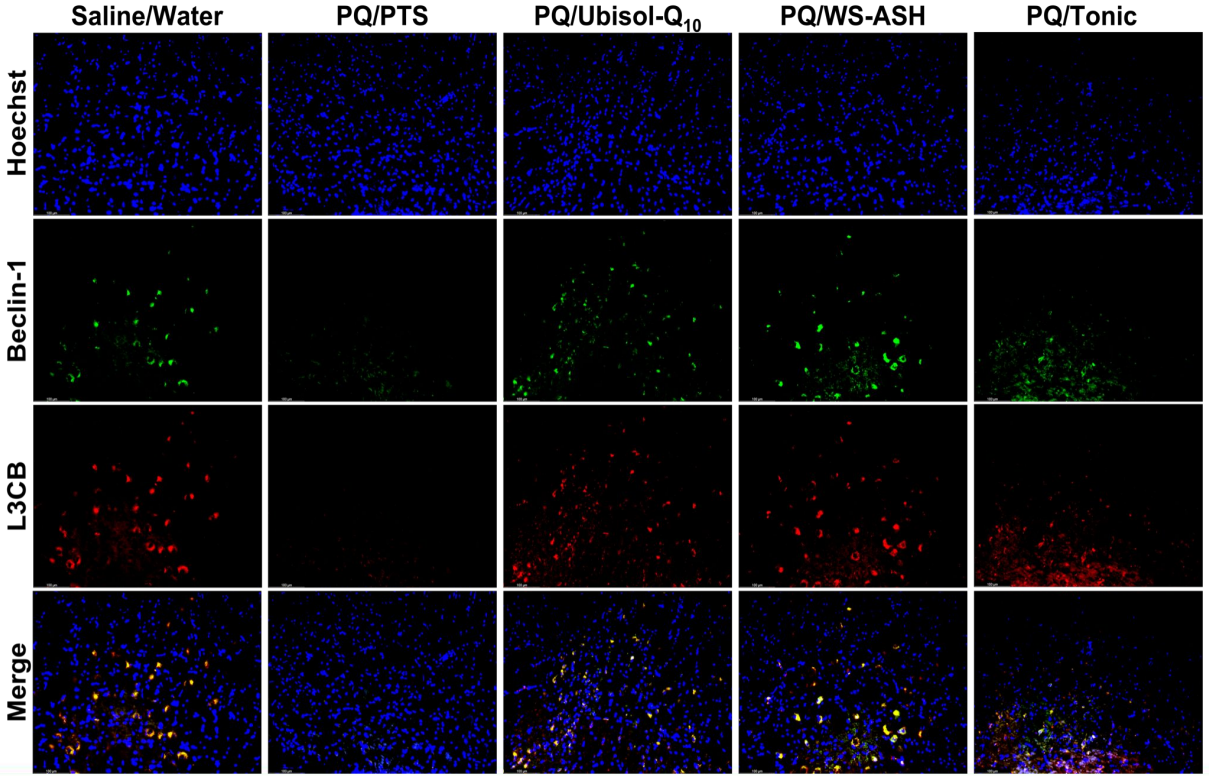
Evaluated:

- ➔ Oxidative stress
- ➔ Autophagy
- ➔ Inflammation
- ➔ Activation of neurotrophic growth factors (NGFs)

Results


Saline/Water
PQ/PTS
PQ/Ubisol-Q10
PQ/WS-ASH
PQ/Tonic
Hoechst
NGF
TH
Merge

Results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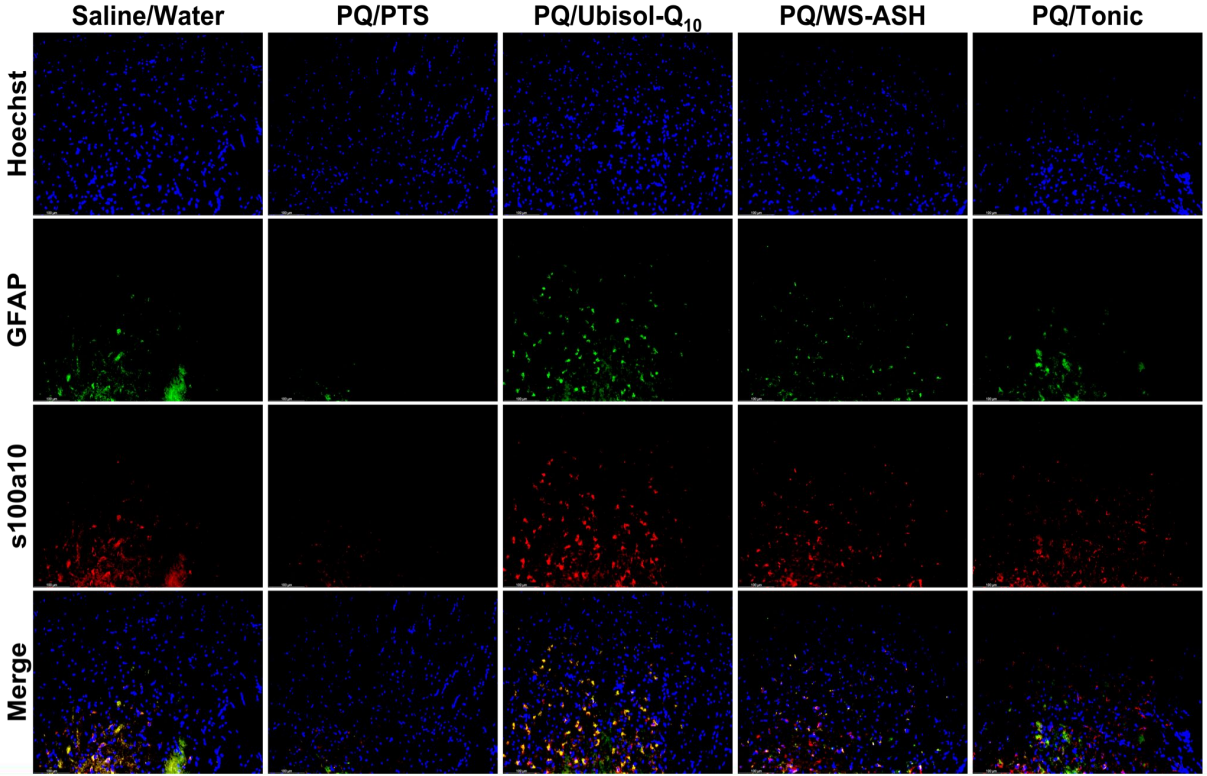
PQ/PTS
PQ/Ubisol-Q10
PQ/WS-ASH
PQ/Tonic
Hoechst
Beclin-1
L3CB
Merge

Results


Saline/Water
PQ/PTS
PQ/Ubisol-Q10
PQ/WS-ASH
PQ/Tonic
Hoechst
GFAP
s100a10
Merge

Summary

- Neuroprotection of dopaminergic neurons in the substantia nigra
- Increased activation of Nerve Growth Factor
- Up-regulation of autophagy mechanisms
- Increased activation of pro-survival astroglial cells

Future Directions

- Quantitative analysis of TH positive neurons in the substantia nigra region using a stereologer

- Evaluate activation of pro-survival neurotrophic factors by immunofluorescent staining of BDNF and GDNF

- Evaluate oxidative stress and senescence in PTS and treatment groups using 4-HNE and p21 antibodies

- Clinical investigation using water-soluble Ashwagandha and Ubisol-Q10

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NSERC CRSNG

next REMEDIES

Mitacs

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