Mechanism based efficacy study of trigonelline based standardized fenugreek seed extract (TGN) on levodopa induced dyskinesia in 6-hydroxydopamine lesioned rat model of Parkinson’s disease

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INTRODUCTION

- Second most common neurodegenerative disorder.
- Involves loss of dopaminergic neurons and depletion of striatal dopamine.
- ‘Wearing-off’ phenomena and dyskinesia with L-Dopa
- Levodopa induced Dyskinesia (LID) within 4–6 years of initiation of L-DOPA treatment.
- Four million people suffer worldwide with PD and this is expected to double by 2030.1
- Around 90% patients are affected by LID after 9-15 years of initiation of L-DOPA treatment.

RATIONALE

- Amanitdine is the only drug for LID alleviation.
- Trigeminal (IBHB) is reported as:
  - Potent antioxidant properties1-3.
  - Neuroprotective and dopaminergic4.
  - Clinically safe in PD patients on L-DOPA.
- No specific treatment is available for LID therefore IBHB was studied in animal model of LID.

OBJECTIVE

To evaluate the effect of IBHB on LID in 6-OHDA lesioned rat model of Parkinson’s disease

RESULTS

RAEPPLEMO

Effect of IBHB on Total AIMS (AIDS) and PAS. Data was analyzed by two way ANOVA followed by Dunnett’s multiple comparisons test (t=7), #p<0.01 as compared with Sham group and ***p<0.001 as compared with LID control. Values in Parenthesis indicates dose in mg/kg.

CONCLUSION

- IBHB significantly reduced the severity of symptoms LID (reduced AIDS).
- IBHB do not interfere with efficacy of L-dopa against PD symptoms (No effects in FAS test).

PROPOSED MECHANISM

Reduced LID-induced mitochondrial energy demand in mitochondria (FosB immunoreactivity, striatal gene expression of FosB, Dyn, JunD) Preventing mitochondrial complex I inhibition (reversal of LID induced gene expression PINK1, Parkin, JunD) and Subsequent reduction to oxidative stress

REFERENCES


2nd INTERNATIONAL CONFERENCE ON HERBAL AND SYNTHETIC DRUG STUDIES, HSDS-2014, (10 -12th Feb 2014).