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EVALUATION OF LIQUORICE ROOT EXTRACT ADMINISTRATION ON ROTENONE INDUCED PARKINSON'S MODEL IN WISTAR RATS

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ABSTRACT

Parkinson's disease is a neurological disorder characterized by motor and nonmotor dysfunction due to loss of dopaminergic neurons in substantia nigra. Rotenone has been shown to induce Parkinson like symptoms in humans. The study was performed to assess the effect of liquorice root extract (LRA) on rotenone-induced Parkinson like symptoms in the Wistar rat model.

Six groups of ten male rats each, were used in the study and included a vehicle control (0.5% CMC), a rotenone only control (2 mg rotenone/kg b. wt., liquorice root extract treated groups (150 and 600 mg/kg b. wt.) and positive control groups (Glycyrrhizin - 40 mg/kg b.wt. and Levodopa – 20 mg/kg b.wt; references of reducing symptoms). For all groups except the vehicle control, the rats received a single intraperitoneal dose of 2 mg rotenone /kg b. Wt. The route of administration for liquorice and positive controls was oral gavage. The duration of treatment was 28 consecutive days.

Measured parameters included grip strength, locomotor activity, catalepsy, postural instability and assays of lipid peroxidation, dopamine, glutathione and superoxide dismutase from brain and plasma as well as brain pathology. Rotenone alone administration leads to significantly reduced grip strength and significantly increased score of catalepsy, postural instability and neurodegeneration compared to liquorice high dose and positive control groups. Rotenone related effects were subsided in animals that received either the positive controls or high dose of liquorice. In liquorice root extract treated high dose group as well as positive control groups, a significantly lower incidence and severity of lesions in brain histopathology supported with significantly reduced alterations in levels of superoxide dismutase, lipid peroxidation and dopamine compared to group treated with rotenone alone. Based on results of this study, Liquorice root extract was found to reduce the neurodegeneration caused by rotenone and may have possible therapeutic effects in treatment of Parkinson's disease.

INTRODUCTION

Parkinson's disease (PD) is a neurological disorder characterized by Motor and Non Motor dysfunction due to loss of dopaminergic neurons resulting in an imbalance between dopamine (an inhibitory neurotransmitter) and Acetyl (excitatory neurotransmitter) level in substantia nigra (SN) developing following signs:

Tremor, Rigidity , Akinesia/Bradykinesia, Postural instability

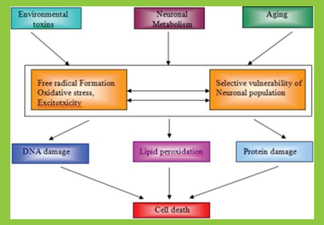
For the majority of individuals with PD, the cause remains unclear. Some research suggests a genetic cause for PD. Environmental toxins, or a combination of toxins and genetics, are also under consideration as possible underlying causes of Parkinson's disease in some patients.

EXPERIMENTAL DESIGN: ROTENONE MODEL OF PD

Group N°	Treatment	Test Drugs	Dose (mg/kg b. wt.)	N° of Male Rats
G1	Vehicle Control	0.5% CarboxyMethyl Cellulose	0	10
G2	Test Drug	Liquorice Extract+ Rotenone	15	10
G3	Test Drug	Liquorice Extract + Rotenone	600	10
G4	Positive Control	Glycyrrhizin+Rotenone	20	10
G5	Positive Control	Levodopa+Rotenone	20	10
G6	Negative Control	Rotenone	2.5	10

Note: Route of administration for all test drugs was Oral Gavage; Rotenone injected intraperitoneally.

PATHOPHYSIOLOGY OF PARKINSON'S DISEASES



WHY ROTENONE FOR INDUCTION OF PD?

- Generates Oxidative stress which results in dopamine metabolism
- Mitochondrial dysfunction occurs as a result of complex I inhibition activation of microglial NADPH oxidase which produces superoxide anion (ROS) and cytokines (TNF-α and IL-1β)
- Leads to the activation of apoptotic cascades in SN neurons leading to Dopaminergic neurodegeneration.
- Unlike other models it reproduces most of the movement disorder symptoms and the histopathological features of PD including Lewy bodies
- Rotenone is a powerful inhibitors of mitochondrial respiration
- Involved in the higher incidence of sporadic Parkinsonism among the population of rural areas

WHY LIQUORICE EXTRACT FOR TREATMENT OF PD?

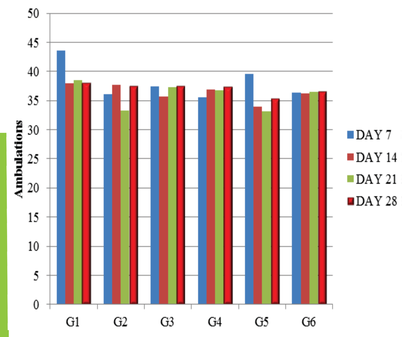
- Liquorice-root contains glycyrrhizin, isoliquiritigenin, and glycyrrhetinic acid. It is proved to prompt a neuroprotective effect in various models.
- Glycyrrhizin also induces antidepressant activity, due to elevation of adrenaline and Dopamine.

OBSERVATIONS

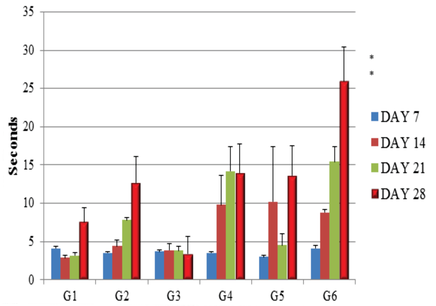
Observation	Frequency
Mortality and morbidity	Twice a day
Clinical signs	Twice a day
Body weight	Days 1 and at 8, 15, 22, 29 day
Food consumption	Days 1 and at every alternate day
Motor parameters	At 0 h (pretreatment, within 8 h of first dosing, at 24 h for first dosing. Then on 7th and 14th, 21 and 28 post dosing day
Biochemical investigation	Every day at pre-post of treatment
Histopathological Examination	At the end of treatment, for each group

RESULTS

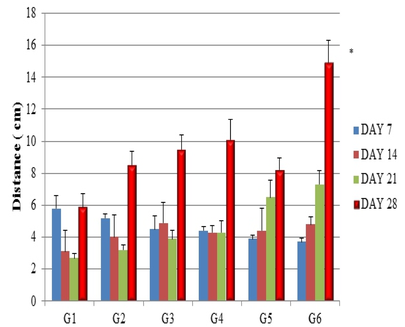
EFFECT OF LRE IN LOCOMOTOR ACTIVITY



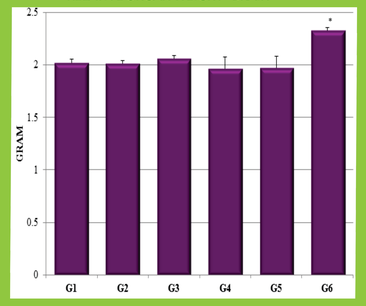
CATALEPSY



POSTURAL INSTABILITY TEST

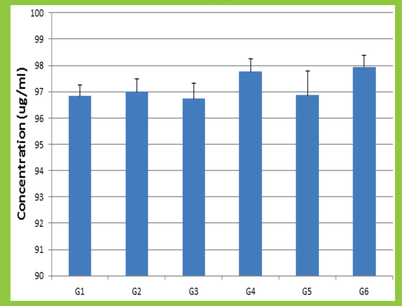


RELATIVE ORGAN WEIGHT - BRAIN

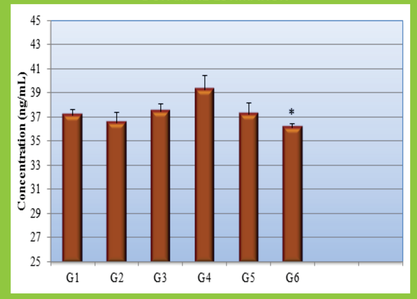


LIPID PEROXIDATION

SOD



DOPAMINE ESTIMATION



CONCLUSION

- Rotenone induced a Parkinson like disorder with similarity to the human disease.
- Liquorice extract at 600 mg/kg reduced the neuro-degeneration and prevented the motor function deterioration caused by rotenone.
- Improvement due to LRE was equivalent to that of L-DOPA (20 mg/kg).
- LRE Prevented the oxidative damage caused by rotenone.
- LRE can be added to other therapies to decrease the progression of disease probably by its antioxidant and neuro-protective effect.