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Comparative Evaluation of Combination of Extracts of *Centella asiatica* and *Glycyrrhiza glabra* for Presentation of Haloperidol Induced Catalepsy

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ABSTRACT

Patient with the Parkinsonism experiences momentary difficulties since in such patients combination therapy is advised. Interaction with these drugs can complicate clinical managements so in present work investigate influence of *Centella asiatica* and *Glycyrrhiza glabra* in combination which were shown promisingly effects in such cases than individual effect.

Extracts of *Centella asiatica* 200 mg/kg and *Glycyrrhiza glabra* 300 mg/kg were orally administered 30 min prior to the intraperitoneally haloperidol 1 mg/kg for acute and chronic period of time to albino mice of either sex similarly scopolamine 1mg/kg administered for other group of animals before haloperidol injection.

Acute as well as chronic co administration of combination of above drugs showed significant reduction in catatonic scores, combination of *Centella asiatica* and *Glycyrrhiza glabra* showed magnificent results so co administration of above extracts in various combinations is highly useful. Number of herbal drugs shows promising effects to control catatonic responses in experimental models of catatonia.

Keywords- Catatonic response, Haloperidol, *Centella asiatica*, *Glycyrrhiza glabra*.

INTRODUCTION

Ayurveda provides the knowledge of healthy living and not merely confined to treatment of the diseases or disorders[1]. Neuroleptics are commonly used in treatment of schizophrenia and other affective disorders[2] are often associated with extra pyramidal side effects[2,3]. Cataleptic immobility can be seen in the rodents by

induction of typical neuroleptics (haloperidol)[4]. Catalepsy by haloperidol occurs due to the blocked of D2 receptor and reduced dopaminergic transmission.

Parkinson's disease is neurodegenerative disorder characterized by the selective loss of dopamine neuron (DA) in substantia nigra pars compacta (SNPc)[5,6]. Hence catalepsy in animal model to screen antiparkinsonian drugs[5-9]. brahmi is well known ayurvedic drug used for the number of CNS complications as failing memory, insomnia, depression stress and epilepsy[10] and liquorice is used as demulcent antacid, antiulcer[11], anti inflammatory, expectorant, tonic diuretic, laxative and sedative[12], antimicrobial, antiherpes[13], anxiolytic[14], antipyretic[15]. brhami and liquorice both are the CNS acting drugs[7], with this back ground information we designed to work on the combinations of these drugs by considering pharmacological properties. Both the plants are still used as the brain tonic and made used in the brains preparations. Both the drugs are traditionally used in the various ailments of CNS. Neuroleptic induced catalepsy has long being used for the screening of the anti parkinsonian activity there is considerable blocked of DA transmission produce catalepsy in rats and extra pyramidal side effect in human. Catalepsy is define as the failure of the animal or human to correct the external posture this is use for the evaluation of the drugs on the extra pyramidal symptoms.

The theories implicate the central cholinergic dysfunction GABA dysfunction; oxidative stress and 5- hydroxyl tryptamine dysfunction have been proposed. Haloperidol blocks the D2 receptor and induces catalepsy in animals by reducing transmission of neuronal chemicals in the basal ganglion.

Nootropics are thought to work by altering the availability of the brain's supply of neurochemicals (neurotransmitters, enzymes, and hormones), by improving the brain's oxygen supply, or by stimulating nerve growth. By concentrating on the above means we further studied them for the cataleptic activity.

EXPERIMENTAL DESIGN

The study protocol was approved by the institutional animal ethical committee.

Drugs

Haloperidol (RPG live sciences) and scopolamine (Cadila health care Ltd) injections were used. *Centella asiatica* and *Glycyrrhiza glabra* extract prepared by percolation and hot extraction respectively.

Collection of the plants

Plants like *Centella asiatica* collected from the medicinal plant garden of the K.L.E.S.'S. College of pharmacy, Belgaum. And roots and rhizomes of Glycerrhiza glabra collected from Amrut kesari depot, Banglore and these were authenticated by the Regional research center Neharu nagar Belgaum.

Extraction process

The Leaves of *Centella asiatica* are shed dried and powder of *Centella asiatica* Leaves was passed through sieve no 40 and extracted by percolation using 70% ethanol (100 gm in 500 ml) at room temperature for 24 h. After filtration, dark green coloured solution obtained from the *Centella asiatica* was evaporated at 50°C under reduced pressure, and then lyophilized (1mg of dry extract of *C. asiatica* leaves is equivalent to 5.26 mg of dried leaves of *C. asiatica*) The roots and rhizomes of *Glycyrrhiza glabra* were crushed to coarse powder and extracted with ethanol (70% v/v) using soxhlet extractor for 24 h. The extract was concentrated under reduced pressure and air dried. The semisolid mass obtained and

stored in an air tight container in refrigerator for further use.

Animals

Male albino mice (25-30g) of either sex procured from M/s. Venkateshwara Enterprises, Bangalore (CPCSEA Reg. No. 276) were used with the approval of the Institute Animal Ethics committee. Animals were reared and maintained at the animal house of the institution and were on standard pellet diet and water *ad libitum*. They were initially acclimatized to the laboratory environment for one week prior to their use. Each group of animals was housed separately, with a distinct identity throughout the study.

Acute study

In acute study animals divided into three groups of six each. The first group received vehicle served as control (C), second group received scopolamine (1mg/kg; ip) and third group received *Centella asiatica* extract (200 mg/kg, orally) and *Glycyrrhiza glabra* extract (300 mg/kg). All drug solutions are freshly prepared and given orally by using feeding tube. Haloperidol (1mg/kg) constituted in normal saline was administered intraperitoneally to induce catalepsy, 30min after vehicle/drug administration[17]. The degree of catalepsy was measured at 5, 15, 30, 45, 60, 90 and 120 min after haloperidol injection. Catalepsy was measured as the time the animal maintained an imposed position with both front limbs raised and resting on 4cm height. The end point was considered to occur when both front paws were removed. If animal fails to correct the posture in 10 seconds from 4cm height, 0.5 score is given for each paw and 0.5 score is given to animal which moves only when touched or pushed. Thus for single mouse maximum possible score would be 3.5 min revealing total catatonia[17].

Chronic study

Centella asiatica extract (200 mg/kg, orally) and *Glycyrrhiza glabra* extract (300 mg/kg), scopolamine (1mg/kg) and vehicle were administered orally once a day to respective groups for 6 more days. Thirty minutes post oral administration, haloperidol (1mg/kg) was administered ip to all groups once daily for 6 more days. Catalepsy again measured on seventh day at 5, 15, 30, 45, 90 and 120 min post haloperidol administration[17].

RESULTS

Acute study (Table-1) in the acute study, administration of the standard drugs and all doses of the test drug gave cataleptic scores similar to that of vehicle treated group. However from comparison of the treated group to the standard drug, scores start to decline from 45 minute onwards on the other hand comparison of control to treated shows reduction in scores significantly after 45 minutes. After administration of haloperidol all doses of CAE+GGE significantly lowered the cataleptic scores compared to the standard as well as control. In fact 45 minutes post haloperidol onwards combination of extract proved to be more protective against haloperidol induced catalepsy, which is significantly nearer to the scores shown by standard drug scopolamine.

Table-2 chronic study, administration of standard drugs and doses of the test drugs 15 minutes after the last haloperidol dose on the 7th day gave cataleptic scores less to that of the vehicle treated group however from 15 minutes onwards after haloperidol administration al doses of standard and test drug resulted in significantly lower cataleptic scores than vehicle treated mice. The result of chronic study shows that the CAE and GGE combination has protective effect against haloperidol induced catalepsy thus

protective action can be found time dependent from the above study.

DISCUSSION

Typical neuroleptic agents such as chlorpromazine, haloperidol, and reserpine induce cataleptic state in rodents which is widely used as a model to test the extra pyremidal side effects of the antipsychotic agent various neurotransmitters like dopamine, ach, serotonine, angiotensine, or opoids have been implicated in catalepsy induced by neuroleptic agents. proof indicate the drugs which trigger the catalepsy rodents may reduce or aggravate extra pyremidal side effects in humans .in present study CAE+GGE combination protected mice from catalepsy induced by haloperidol as effectively as standard drug scopolamine. In earlier study we found both drugs effective in neurological disorders the anti cataleptic effect of both drugs are may be due to their nourishing and antioxidant property however further study is require further glance on the effective principals from both extracts. From above study drug can be suggested for alternative adjuvant therapy.

Acute study

Significant reduction in the catatonic score are observed after some time intervals of 45 minutes a- $p < 0.05$, when compared with normal animals. b- $P < 0.01$, when compared with control animals.

CONCLUSION

From the above study, it has been concluded that acute as well as chronic co-administration of combination of *Centella asiatica* and *Glycyrrhiza glabra* drugs showed significant reduction in catatonic scores, combination of above showed magnificent results so that co-administration of above extracts in various combinations is highly efficient. *Centella asiatica* and *Glycyrrhiza glabra* shows promising effects to control catatonic responses in experimental models of catatonia.

REFERENCES

1. Ganachari MS, Veeresh Babu SV, Katare SS. Neuropharmacology of an extract from *Centella asiatica*, *Pharm biol*, 2004,Vol. 42 (3), 246-252.
2. Pemminati S, Nair V, Dorababu P, Effect of ethanolic leaf extract of Oscimum sanctum on haloperidol induced catalepsy, *Ind J Pharmacol* 2007, Vol 39(2), 87-89.
3. Kulkarni SK, Naidu PS, Tradive dyskinesia: An Update. DrugsToday 2001, 37:97-119.
4. Rang HP, Dale MM, Pharmacology, Churchill livingstone, 5th edition, 2003, 497-501, 476-486.
5. Goodman JG, Limbird LE, The pharmacological basis of therapeutics, 10th edition, Mcgraw Hill Publication, 294-549.
6. Copra RN, Nyar SL, Chopra IC. Glossary of Indian Medicinal Plants. CSIR, New Delhi, 1956, 217.
7. Chaterjee A, Pakrashi SC 1995: The treatise on Indian medicinal plants. Vol 4 PID, New Delhi, 33-35.
8. Benbadis SR. Epileptic Seizures and Syndromes. *Neurologic clinics*, 2001; 19(2):251-70.
9. Waxman SG. Epilepsy, chapter 21 in: correlation neuron anatomy 23 rd, Appleton and lange A simon Schuster company, Stanford, 1996; 280-82.
10. Vogel HG, Wolf GH, Antiepileptic activity chapter E-3 In drug discovery and evaluation, Springerverlage, Berlin 1997, 246-66
11. Mcnamara J. drugs effective in the therapy of epilepsy, chapter 21 In: Goodmann and Gilmann's the pharmacological basis of therapeutics. Hardman GJ. Al. Mcgrew hill company Inc. New York, 2001, 521-47.
12. Boglicum G, Beghi E. Anticonvulsant Drugs and Bone Metabolism. *Acta Neurol Scand* 1986; 74:284-88.
13. Ambawade SD, kasture VS, Kasture SB. Anxiolytic activity on Glycerrhiza glabra linn. *J Natural Remedies* 2001, 2, 130-134.

14. Malhotra R. Compendium of Indian medicinal Plants. CSIR: New Delhi. 1995 - 173.
15. Handa SS, Mangal AK. Indian Herbal Pharmacopoeia (Vol I). *Indian Drugs Manufacturer Association, Mumbai*. 1998-47.
16. Sertia JA, Camargo EA, Lucia RD, Panizza S. Pharmacology and toxicology of *Centella asiatica* extract. *Fitoterpia*. 1997; 68: 413-416.

Table 1. Effect of *Centella asiatica* and *Glycyrrhiza glabra* extracts reduces the catatonic responses induced by haloperidol (Acute study)

Groups	Cataleptic scores at different time points (min)						
	5	15	30	45	60	90	120
Control	1.5 ±0	1.41±0.27	1.91±0.32	1.75 ± 0.17	2.25 ± 0.28	2.58 ±0.15	2.58±0.15
Standard	0.41± 0.08 [b]	0.5 ±0[a]	0.25 ± 0.11[b]	0.16 ± 0.10[b]	0.16 ±0.10[b]	0.33± 0.10[b]	0.25±0.11[b]
Treatment	0.58±0.15[b]	1± 0.22	1.25 ± 0.17	1.25 ± 0.10	1.16 ± 0.10[b]	1.08± 0.08[b]	0.91±0.15[b]
	F-33.41 P<0.01	F- 5.112 P - 0.01	F-14.21 P- 0.001	F-28.3 P<0.01	F- 32.12 P<0.01	F-94.5 P<0.01	F-72.56 P<0.01
Statistical analysis by One- way ANOVA followed by Dunnett's Multiple Comparison Test							

a- $p < 0.05$, when compared with normal animals.
b- $p < 0.01$, when compared with control animals.

Table 2. Effect of *Centella asiatica* and *Glycyrrhiza glabra* extracts reduces the catatonic responses induced by haloperidol (Chronic study)

Groups	Cataleptic scores at different time points (min)						
	5	15	30	45	60	90	120
Control	1 ± 0.22	1.5 ± 0	1.75 ± 0.11	2 ± 0	1.75± 0.11	1.6±0.10	1.83±0.10
Standard	0.41 ± 0.08 a	0.41±0.083 b	0.083±0.08 b	0.25±0.1 b	0.25±0.11 b	0.25 ±0.11 b	0.08± 0.08 b
Treatment	0.16 ± 0.10 b	0.25 ± 0.17 b	0.25± 0.11 b	0.25±0.11 b	0.16± 0.10 b	0.16± 0.10 b	0.08± 0.08 b
	F- 8.061 P>0.05	F-38.27 P<0.001	F-79.13 P<0.001	F-122.5 P<0.001	F-65.96 P<0.001	F- 61.4 P<0.001	F-122.5 P<0.001
Statistical analysis by One- way ANOVA followed by Dunnett's Multiple Comparison Test							

a-$p < 0.05$, when compared with normal animals.
b-$p < 0.01$, when compared with control animals.