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Effect of Various Extracts of *Momordica charantia* Pulp and Seed on Clonidine and Haloperidol-Induced Catalepsy in Mice

Maharudra Rakh*, Adinath Munde, J Banurekha, M Kumar, Dr. V. Muruganantham, B S Venkateswarlu

Department of Pharmacy, Vinayaka Mission's College of Pharmacy, Salem, Tamil Nadu, India
***Address correspondence to:** E-mail address: rmspharma@gmail.com

ABSTRACT

The present study sought to determine, in more detail, the effects of various extracts of Momordica charantia pulp and seed for anti-cataleptic activity as the plant is having antiasthamatic activity. The cataleptic response of mice to various extracts of Momordica charantia pulp and seed measured using a bar test, was enhanced by subcutaneous pretreatment with Clonidine (1 mg/kg). Methanol extract and Aqueous extract (50 mg/kg, i.p.) of the plant more significantly inhibited clonidine-induced catalepsy as compare to petroleum ether and ethyl acetate but not any one extract among these inhibited haloperidol-induced catalepsy for both the parts of plants. Thus the antihistaminic activity of Momordica charantia pulp and seed may be due to polar constituents.

Key words: *Momordica charantia,* cataleptic activity, antiasthamatic, clonidine, haloperidol.

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INTRODUCTION

Momordica charantia climbing creeper plant fruits and leaves are traditionally used as medicinal agent of asthma, leprosy, bronchitis, fever, tridosha [1]. Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining normal posture. Catalepsy is a sign of extrapyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain. Clonidine, α_2-adrenoceptor agonist, induces dose dependent catalepsy in mice, which is inhibited by histamine H_1 receptor antagonists but not by H_2 receptor antagonist [2]. They also showed that pretreatment with L-histidine, a precursor of histamine potentiated clonidine-induced catalepsy in dose dependent manner. Muley et al., (1979) showed that intracerebroventricular injection of histamine in conscious mice induced catalepsy, which was inhibited by H_1 receptor antagonist but not by H_2 receptor antagonist [3]. It is known that clonidine releases histamine from mast cells [4]. Schwartz (1997) identified histamine containing mast cells in brain [5]. Clonidine-induced release of histamine from mast cells is inhibited by α_2–adrenoceptor blocker, prazocine [6]. Neuroleptic agent also induced catalepsy, but by different mechanism. Neuroleptics inhibit dopamine D_2 receptors in the substantia nigra [7,8]. Therefore it was our objective to study the effect various extracts *Momordica charantia* pulp and seed on clonidine-induced catalepsy, as it is used traditionally in cough, asthma and inflammation [9]. Since catalepsy is a common extrapyramidal side effect of neuroleptic agents and the effect of the plant on haloperidol-induced catalepsy is not known, we also studied their effect on haloperidol-induced catalepsy in mice.

MATERIAL AND METHODS

Plant Material

Momordica charantia were collected from Therla, Ta. Patoda, Beed district of Maharashtra in September 2020 and authenticated by D.L.Shirodkar, Botanist, Botanical Survey of India, WRC, Pune, where a sample specimen (voucher number: RMS 03 and RMS 04) No. BSI/WRC/IDEN.CER./2020/H1 has been deposited.

Extraction

Dried and coarsely powdered pulp and seed of *Momordica charantia* was subjected to successive solvent extraction in Soxhlet extractor using petroleum ether, ethyl acetate, and methanol as solvent and the marc left was refluxed with water. *Momordica charantia* pulp extracts were vacuum dried to produce Petroleum ether (1.27%), Ethyl acetate (4.04%), Methanol (13.77%) and Aqueous (4.52%) extracts; *Momordica charantia* seed extracts were vacuum dried to produce Petroleum ether (3.02%), Ethyl acetate (2.04%), Methanol (11.54%) and Aqueous (4.58%) extracts respectively.

Animals

Male albino mice (Swiss strain) weighing 25-28 g were housed under standard laboratory conditions, five in each groups. The animal had free access to food with standard pellet diet (Amrut laboratory animal feed, Sangali, M.S.) and water ad libitum. The animals maintained under standard husbandry conditions and had free access to diet and water. The animals were fasted overnight prior to the experiments. The distribution of animals in the groups, the sequence of trials and the treatment allotted to each group were randomized, throughout the experiment. All the experiments were approved and conducted as per the guidelines of Institutional animal ethical committee. (DYPCOP/IAEC/2020/06)

Drugs and Chemicals

The following drugs and chemicals were used. Drugs: Clonidine (Neon Lab. Ltd., India), Haloperidol (Sun pharma, India), Pheniramine maleate (Unimark Remedies Ltd., India) purchased from commercial source. Chemicals: petroleum ether (60-80°C) (RFCL Ltd, India), ethyl acetate (RFCL Ltd, India), methanol (MERCK Ltd, India), and DMSO (Research Lab Industries, India).

Assessment of Anti-cataleptic Activity [10-14]

Bar test was used to study the effect of various extracts on clonidine-induced catalepsy. Clonidine (1 mg/kg, s.c.) was injected to mice (n = 5) pretreated 30 min before with vehicle (5 ml/kg, i.p.), petroleum ether, ethyl acetate, methanol, and aqueous extracts of *Momordica charantia* pulp and seed (50 mg/kg, i.p., each) or standard drug pheniramine maleate (10 mg/kg, i.p.). The dosages were selected based on preliminary studies (data not shown). The forepaws of mice were placed on horizontal bar (1 cm in diameter, 3 cm above the table) and the time required to remove the paws from bar was noted for each animal and the durations of catalepsy was measured at 30, 60, 90, 120, 150 and 180 min. The standard bar test was used to determine the intensity of catalepsy (e.g. Hoffman & Donovan, 1995). Both forelegs of a mouse were placed on a horizontal bar. The latency from paw placement until the rest complete removal of one paw from the support was measured (maximal test duration, 180 s) and termed here as descent latency. If the mice did not assume the position on the bar after three attempts, it received a descent latency of 0 s.

Effect on Haloperidol-Induced Catalepsy [10-13]

The same Bar test was used using haloperidol. Haloperidol (1 mg/kg, i.p.) was injected to mice (n = 5) pretreated 30 min before with vehicle (5 ml/kg, i.p.), petroleum ether, ethyl acetate, methanol or aqueous extracts of *Momordica charantia* pulp and seed (50 mg/kg, i.p., each). The durations of catalepsy was measured at 30, 60, 90, 120, 150 and 180 min.

Statistical Analysis

The data is presented as mean ± SEM. The data was analyzed by one-way ANOVA followed by Dunnet's test. $P< 0.01$ and $P<0.05$ was considered significant.

RESULTS

Clonidine Induced Catalepsy

All the extracts of *Momordica charantia* pulp and seed for petroleum ether, ethyl acetate, methanol and aqueous ($P<0.05$) extracts showed significant inhibition in catalepsy (Table No. 1). But among them methanol and aqueous extracts shows more significant inhibition in catalepsy. Results were comparable with control drug clonidine.

Haloperidol-Induced Catalepsy

None of the extracts of *Momordica charantia* pulp and seed for inhibited haloperidol-induced catalepsy (Table No. 2). Results were comparable with control drug haloperidol.

DISCUSSION

Several drugs are known to induce catalepsy in animals. The neuroleptic agents induce catalepsy by inhibiting dopamine D_2 receptors in the substantia nigra [7]. Chopra and Dandiya (1975) have studied the relative role of acetylcholine and histamine in perphenazine-induced catalepsy and suggested that anticholinergic activity of antidepressant might be due to an increase in dopamine content in brain or their ability to inhibit release of acetylcholine [15]. They also showed that different stages of catalepsy to be directly correlated with brain histamine content. Uvnas (1969) studied the mast cell degranulation and its correlation with the release of histamine after administration of mast cell degranulating agent (Compound 48/80) [16]. Lakdawala et al., (1980) have shown that clonidine releases histamine from mast cells in a similar manner to a selective liberator like compound 48/80.[4] Haloperidol, a typical neuroleptic produces catalepsy in rodents and extrapyramidal side effects in human [17]. Haloperidol-induced catalepsy is one of the animal models for testing the extrapyramidal side effects of antipsychotic drugs. Haloperidol, (a non-selective D_2 dopamine antagonist) induced catalepsy is primarily due to blockade of dopamine receptors in the straiatum. The agents increasing dopamine transmission inhibits neuroleptic-

induced catalepsy. The straiatum and nucleus accumbens have been implicated as the major brain structures involved in antipsysychotic induce catalepsy, which appears due to the blockade of dopamine neurotransmission [18]. Typical neuroleptic-induced catalepsy has been linked to a blockade of postsynaptic striatal dopamine D_1 and D_2 receptors [7,19]. Despite this evidence, dysfunction of several other neurotransmitters such as acetylcholine [20], GABA [21] and serotonin [22], have also been implicated. In addition to dysfunction of various neurotransmitters in catalepsy, many clinical and preclinical studies have suggested the involvement of reactive oxygen species in haloperidol induced toxicity [23,24]. The observation of this study indicated that the plant *Momordica charantia* pulp and seed having antihistaminic activity inhibited clonidine-induced catalepsy and not inhibited haloperidol-induced catalepsy. From the present study we can conclude that the cataleptic effect of clonidine in the mouse is mediated by histamine release from mast cells and the clonidine-induced catalepsy was inhibited by methanol and aqueous extract of *Momordica charantia* pulp and seed. The effect of these extracts on clonidine-induced catalepsy is probably due to their mast cell stabilizing property and the plants do not have activity on dopaminergic transmission. Aqueous extract of *Momordica charantia* pulp and seed showed most potent inhibition of clonidine-induced catalepsy so it can be concluded that polar constituents may be responsible for its antihistaminic activity.

Table No. 1: Effect of various extracts of *Momordica charantia* pulp and seed on clonidine-induced catalepsy in mice

Sr. No.	Group/ Extract	Plant Part	Duration of catalepsy (sec) Mean ± SEM at					
			0min	30min	60min	90min	120min	180min
1	Control	-	18.6±0.87	226.3±9.55	208.8±26.38	21.5±0.65	17.6±0.98	15.2±1.32
2	Standard	-	16±0.32	25.5±1.76	43.5±1.44	22.75±0.85	18.2±0.20	15.2±1.11
3	Petroleum ether	Pulp	9±7.64	14±8.2**	21±6.4**	25± 5.80	16±6.18	11±8.48
		Seed	34±6.5	57± 7.8**	59± 2.67**	19± 6.6	18± 5.6	13± 4.8
4	Ethyl acetate	Pulp	12±5.3	52±7.2**	56±3.2**	23±6.4	12±7.7	11±3.54
		Seed	26± 6.18	37± 7.2**	48± 4.3**	17± 2.37	13± 5.67	8± 5.46
5	Methanol	Pulp	16±4.9	67±4.5**	49±5.72**	56± 6.16**	42±2.4**	14±5.4
		Seed	24± 6.13	42± 5.2**	52± 6.1**	14± 5.61	12± 2.4	9± 1.44
6	Aqueous	Pulp	36±7.64	43±1.84**	19±1.55**	15± 1.34	12±2.67	10±2.65
		Seed	14± 5.86	12± 7.65**	11± 4.34**	7± 5.22	6± 2.65	3± 3.34

Data are expressed as Mean ± S.E.M, n = 5 in each group, Statistical analysis done by one way ANOVA followed by Dunnett's test. **p<0.01, compared to control group.

Table No. 2: Effect of various extracts of *Momordica charantia* pulp and seed on haloperidol- induced catalepsy in mice

Group/ Extract	Plant Part	Duration of catalepsy (sec) Mean ± SEM at					
		0min	30min	60min	90min	120min	180min
Control	-	31.75± 7.157	41.5±.398	66± 12.213	48.5± 8.874	49± 4.546	39.75±8.350
Standard	-	21.25± 7.284	51.5±5.315	57.75±9.911	136± 6.976	72.25±4.479	68.75±8.901
Petroleum ether	Pulp	39.25± 4.851	19.25± 6.583	23.75±5.954	34± 4.555	29.67±6.098	21± 8.371
	Seed	115.8± 2.873	81.25± 1.632	71.75±7.574	71.5± 6.756	68.75±4.868	53.25±4.540
Ethyl acetate	Pulp	40.5± 1.386	48.5± 4. 455	78.5± 4.293	59± 4.287	38.75±7.638	24.25±4.239
	Seed	115.8± 2.972	110± 2. 576	121± 2.242	111.75±3.88	58± 4.674	47.25±2.485
Methanol	Pulp	57.5± 4.266	45±8.674	28.25±1.174	61.25±8.586	49.5± 7.768	25.5± 7.328
	Seed	25± 5.967	30.75± 6.808	123± 2.385	67± 6.772	38.75±9.176	31.75±2.763
Aqueous	Pulp	114± 6.222	11.67± 4.273	26.67±7.276	59± 4.467	49.67±3.783	21.67±4.847
	Seed	65± 4.342	14± 5.459	98± 4.274	47± 5.878	26± 5.258	21± 6.872

Data are expressed as Mean ± S.E.M, n = 5 in each group, Statistical analysis done by one way ANOVA followed by Dunnett's test, compared to control group.

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CONFLICTS OF INTEREST
Nil

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