INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

EVALUATION OF NEUROLEPTIC ACTIVITY OF PIPERINE ON PSYCHOSIS INDUCED SWISS ALBINO MICE

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Article Received on: 15/09/18 Approved for publication: 29/10/18

DOI: 10.7897/2230-8407.0911268

ABSTRACT

Psychosis is defined as an abnormal condition of the mind that results in the difficulties telling what is real or what is not. According to the statistics in United States 3% of people develops psychosis at some point in time. In this present study we are going to compare pipernin with the standard drug Aripiprazole. For this we are taking 30 mice which are divided into 5 groups, each group consists of 6 mice. Group 1 is used as normal to which a dose of tween 80(vehicle) 1%v/v was given, group 2 mice are given Amphetamine 2.5mg/kg body wt. for inducing psychosis, group 3 animals are used as standard by giving them 0.5ml Aripiprazole through intra venal route, the group 4 and group 5 animals are used as test which are given different doses of pipernin. A dose of 20mg/kg is given to group 4 and a dose of 40mg/kg is given to group 5. The main parameters that are observed are stereotypic behavior of mice, Locomotory activity of mice, biochemical estimation and cataleptic activity. The results that are observed are in stereotypic behavior is number of sniffing is reduced. Locomotory time was reduced. Catalepsy has shown significant mean cataleptic course. Pipernin 40mg/kg has shown activity almost equal to standard and normal. The biochemical parameter estimated is dopamine in frontal cortex. 40mg/kg has reduced dopamine levels significant compared to that of normal and standard. Further study is required in order to evaluate mechanism of action and drug interaction in pipernin.

Keywords: pipernin, Aripiprazole, Black Pepper and Amphetamine.

INTRODUCTION

Psychosis (schizophrenic, schizoaffective and full of feeling ailments) is a gathering of genuine sicknesses that influence the brain. It is a noteworthy crippling, intricate and expensive ailment that strikes 1% of the total population[1]. Schizophrenia keeps on being a secretive sickness, entrancing the brains of specialists, pharmacologists and neuroscientists everywhere throughout the world for in excess of a century. The essential welfare of the millions tormented with schizophrenia is in question. Schizophrenia is an impairing condition having beginning prior in men (15-25 yrs.) than in ladies (25-35yrs), with a lifetime worldwide pervasiveness of 1%.Congestive side effects show as shortages in consideration, learning and memory. Hyperactivation of mesolimbic pathway and brokenness of mesocortical pathway produces unevenness in the serotonergic, dopaminergic, GABAergic and glutamatergic neurotransmission in certain area of mind, are significant reason of psychosis[2-5]. Different reasons of psychosis can be ascribed to heredity, stretch, oxidative pressure, NMDA receptor enemies, tranquilize misuse and horrendous damage. Antipsychotics are utilized for the administration of psychosis are normal and atypical. Antagonistic impacts because of the utilization of regular antipsychotics is additional pyramidal reactions though, atypical antipsychotic have lesser additional pyramidal symptoms[6]. Regardless of the accessibility of various medications for treatment of psychosis, in any case, at present there is no acceptable cure accessible for aversion and administration of psychosis[7]. Herbals pharmaceuticals are hugely thought to be less dangerous than engineered ones. Presently a-day, there has been developing enthusiasm for the restorative utilization of plants as a result of their sheltered and temperate utilize[8-13]. Subsequently, the point of our examination was to investigate the capability of plant in the administration of psychosis.

The main aim was to induce psychosis in swiss albino mice by giving Amphetamine and to evaluate the neuroleptic activity of piperine by comparing with standard drug(ARI).The selected plant molecule was reported to have many ethnomedicinal values which have paved the interest to evaluate efficacy of piperine. Hence the present drug aims to screen the pharmacological activity i.e., neuroleptic activity of Piperine in different doses.

MATERIALS AND METHODS

Black Pepper, ethanol, piperine and Amphetamine(obtained from Yucca enterprises Pvt. Limited Mumbai, India), Aripiprazole(purchased from CSIR) and Six to seven weeks old female mice(obtained from the animal house of Mahaveer enterprises Hyderabad having the REG.NO 146/99/CPCSEA).

Chemicals and reagents

0.9% NaCl, 1% tween- 80 and 2% Gum acacia.

Amphetamine induced stereotypic behaviour in mice

In this model animals were divided into five groups and each group consisted of six animals. The control animals received normal diet consisting of wheat flour, kneaded with water. All the studies were conducted according to the ethical guidelines of IAEC after obtaining necessary clearance from the committee (Approval No: 009/IAEC). They were arbitrarily appointed to each medication regimen and got the PIP (20mg and 40mg) one hour preceding amphetamine (2.5 mg/kg, i.p) injection. The positive control gather got Aripiprazole (2.90mg/kg ,i.m) 30 min before amphetamine infusion[14]. Swiss pale skinned person mice were at first put separately in round and hollow metal enclosures for 15 min to adapt to the new condition. Promptly after amphetamine organization, the mice were put inside the confine

at its base[15]. After 30 min of amphetamine organization, the creature was put on the internal top of the pen and cover was shut[16]. Amphetamine does not incite unconstrained climbing conduct as apomorphine does and subsequently when the amphetamine treated creature is set on the top of the enclosure, it stayed on it for a more drawn out time while the saline treated creature will promptly go down to the base[17]. The aggregate time spent on the inward top/mass of the pen was estimated for 30min.The force of stereotyped conduct of individual mice was scored at 15 minutes interims for a time of 60 min.

The scoring system used was:
Score 0 (no change compared to control),
Score 1 (discontinuous sniffing, constant exploratory activity),
Score 2 (continuous sniffing, periodic exploratory activity),
Score 3 (continuous sniffing, discontinuous biting, gnawing or licking), and
Score 4 (continuous biting, gnawing or licking; no exploratory activity).

Locomotory activity

The locomotory activity of rats was measured using photoactometer (INCO, Ambala, India).

Catalepsy

Aripiprazole (2.90 mg/kg) was injected i.p. on the 6th day to control mice (n = 6) treated with normal diet consisting of wheat flour, kneaded with water. Different concentrations of test and standard drugs are injected orally and intraperitoneally[18-20]. The length of catalepsy was estimated at 0, 60, 90, 120, 150 and 180 min, utilizing Bar test. Both the forepaws of mouse were set on a flat banish raised 3 cm from the table, and the time required to expel the forepaws from the bar was recorded as the span of catalepsy[21-24]. In every one of the analyses, the spectator was incognizant in regards to the treatment given to the mice. Between tests, the creatures were come back to their home enclosures.

Biochemical Estimation

The animals were sacrificed by cervical dislocation, whole brain was rapidly frozen at -5°C and brain dopamine level was spectro fluorimetrically estimated by the methods of Ansell and Beeson as modified by Cox and Perhach[25-27].

Statistical analysis

Results are communicated as mean ± S.E.M. what's more, the measurable examination of information was finished utilizing one-path investigation of fluctuation (ANOVA), trailed by Tukey test to decide the level of hugeness utilizing Graph cushion crystal. Likelihood level under 0.05 was considered measurably noteworthy[28-30].

Table 1: Grouping of Animals

Group	Animals	Treated with	Days of treatment
I (+ve control)	6	Tween-80 (1%v/v)	6
II (-ve control)	6	Amphetamine (2.5mg/kg B.W.) p.o	6
III (Standard)	6	Aripiprazole (0.05ml i.m)	6
IV (Test-1)	6	Piperine (20mg/kg B.W p.o)	6
V (Test-2)	6	Piperine (40mg/kg B.W p.o)	6

Table 2: Evaluation of neuroleptic activity of Piperine by following models

Model	Group I	Group II	Group III	Group IV	Group V
Stereotypy (sniffing)	17.34±0.4051	32.18±0.5573	9.14±0.2259	16.18±0.3089	14.22±0.3087
Locomotor	795.5±19.07	942.8± 5.958	780.7±29.98	882.5±5.987	772.2±34.91
Catalepsy	0	4.277±0.1954	3.802±0.1792	2.003±0.1535	1.715±0.159
Brain dopamine(FC)	0.425±0.023	0.518±0.022	0.316±0.019	0.405±0.0143	0.33±0.01633

Figure 1: Sniffing behaviour of various models

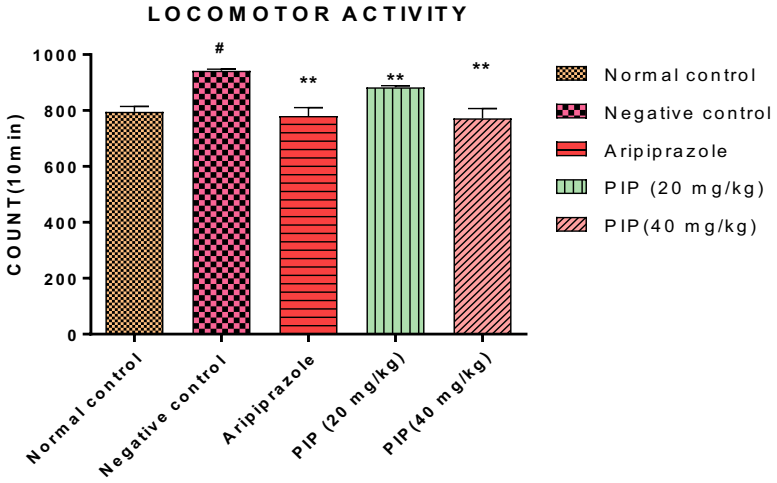

Figure 2: Locomotor activity of various models

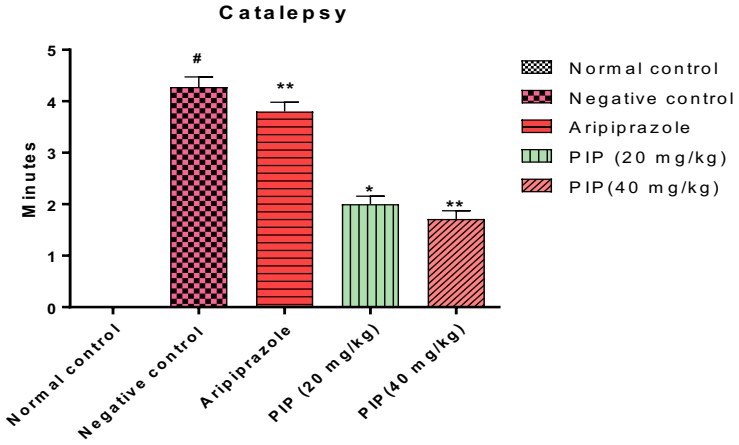

Figure 3: Neuroleptic activity of Piperine using catalepsy model of various models

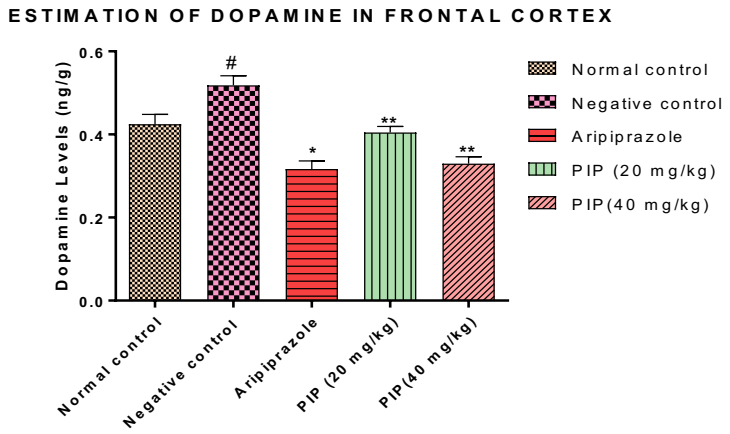

Figure 4: Evaluation of neuroleptic activity of piperine Using biochemical estimationsof various models

RESULTS AND DISCUSSION

Evaluation of neuroleptic activity of piperine using Amphetamine induced stereotypic behaviour in mice model

Amphetamine (2.5mg/kg, i.p) delivered stereotypic conduct in mice. Diverse groupings of PIP(20 &40mg) through oral course astoundingly (p 0.01) diminished this stereotypic conduct of mice created by Amphetamine. Creatures treated with Aripiprazole (2.90 mg/kg, i.m) turned around the stereotypic conduct incited by amphetamine. The impact of PIP was observed to be tantamount to that of Aripiprazole (Antipsychotic agents).

Evaluation of neuroleptic activity of piperine using locomotory model in mice

Administration of PIP (20 & 40mg), through oral route for 6 successive days markedly (p<0.05) decreased Locomotor action in mice estimated utilizing actophotometer. Not withstanding, the convergences of 20mg and 40mg of PIP were astoundingly (p 0.01) powerful in diminishing Locomotory action. The impact of PIP was observed to be similar to that of Aripiprazole (Antipsychotic agents).

Evaluation of neuroleptic activity of piperine using catalepsy model

Animals treated with Aripiprazole (2.90 mg/kg. i.m.) produced the maximum catalepsy at 120 min (235 ± 5.275s). PIP (20 &40mg) through a specially prepared diet, significantly potentiated Aripiprazole induced catalepsy at each time interval, in a dose dependent manner. At dose 20 &40mg shows maximum catalytic score 3.802±0.1792, 2.003±0.1535, 1.715±0.1594 respectively for 120 min of p value (P < 0.01) in Aripiprazole treated animals.

Brain Dopamine Level

Organization of PIP at 20mg &40mg for 6consecutive days indicated especially noteworthy (p 0.05) impact on mind dopamine level. Not withstanding, organization of PIP at the convergence of 20 and 40mg for 6 continuous days indicated strikingly critical (p 0.01) diminish in mind dopamine level in mice contrasted with control.

Schizophrenia keeps on being a puzzling malady entrancing the brains of specialists, pharmacologists and neuroscientists everywhere throughout the world for in excess of a century. In the present investigation, we have centered upon the impacts of effects of piperine on psychosis. Amphetamine-Induced stereotypy is a usually utilized interceptive conduct model to assess antipsychotic capability of any medication. Aripiprazole (antipsychotic operator) was utilized in the present examination as standard antipsychotic specialist. Organization of PIP (20 &40mg/kg)in an uncommonly arranged eating regimen for 6 progressive days in various fixations demonstrated altogether (P 0.05, P 0.01) hindrance of stereotypic conduct in mice as reflected by decreased sniffing and licking behaviour, decrease in locomotory activity, potentiating of Aripiprazole-induced catalepsy and decrease in dopamine levels in brain of mice which has proven that it has anti-psychotic activity.

CONCLUSION

The present examination presumes that the piperine can hinder dopaminergic neurotransmission and conceivably squares dopamine D2 receptor. Therefore, PIP have antidopaminergic movement. The outcomes propose that the PIP may have potential clinical application in the administration of psychiatric disorders. Two test doses of PIP (20& 40mg/kg p.o.) are evaluated using psychosis induced mice in different psychotic induced models and it shows significant inhibition of psychosis with a significance of p<0.01 and p<0.05 when compared with the standard drug ARI (2.90mg/kg i.m.). By the above stated models, PIP (40mg/kg) demonstrated a significant antipsychotic activity than PIP(20mg/kg) when compared with that of standard drug ARI. From our study both doses 20 and 40 mg/kg doses of PIP have shown the neuroleptic activity but not with that of standard drug so, further studies should be carried out to establish exact mechanism of piperine in treating psychosis.

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Cite this article as:

Thammi Reddy Vani *et al*. Evaluation of neuroleptic activity of piperine on psychosis induced swiss albino mice. Int. Res. J. Pharm. 2018;9(11):110-114 http://dx.doi.org/10.7897/2230-8407.0911268

Source of support: Nil, Conflict of interest: None Declared