Ethanolic extracts of Alstonia Scholaris and *Bacopa Monniera* possess neuroleptic activity due to anti-dopaminergic effect

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ABSTRACT

Background: An increased inclination has been observed for the use of herbal drugs in chronic and incurable diseases. Treatment of psychiatric diseases like schizophrenia is largely palliative and more importantly, a prominent adverse effect prevails with the majority of anti-psychotic drugs, which are the extrapyramidal motor disorders. Existing anti-psychotic drug therapy is not so promising, and their adverse effect is a matter of concern for continuing the therapy for long duration. **Objective:** This experimental study was done to evaluate the neuroleptic activity of the ethanolic extracts of two plants *Alstonia Scholaris* and *Bacopa Monnieri* with different anti-psychotic animal models with a view that these plant extracts shall have no or at least reduced adverse effect so that it can be used for long duration. **Materials and Methods:** Two doses of both the extracts (100 and 200 mg/kg) and also standard drug haloperidol (0.2 mg/kg) were administered to their respective groups once daily with 5 different animal models. After that, the concentration of the dopamine neurotransmitter was estimated in two different regions of the brain *viz*. frontal cortex and striatum. **Results:** The result of the study indicated a significant reduction of amphetamine-induced stereotype and conditioned avoidance response for both the extracts compared with the control group, but both did not have any significant effect in phencyclidine-induced locomotor activity and social interaction activity. However, both the extracts showed minor signs of catalepsy compared to the control group. The study also revealed that the neuroleptic effect was due to the reduction of the dopamine concentration in the frontal cortex region of the rat brain. The results largely pointed out the fact that both the extract may be having the property to alleviate the positive symptoms of schizophrenia by reducing the dopamine levels of dopaminergic neurons of the brain. **Conclusion:** The estimation of dopamine in the two major regions of brain indicated the alteration of dopamine levels was the reason for the anti-psychotic activity as demonstrated by the different animal models.

Key words: Alstonia, bacopa monniera, dopamine, dyskinesia, neuroleptic, psychosis

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INTRODUCTION

Incidence of schizophrenia is high, which accounts for almost 1 in every 276 people[1] or precisely 2.5 million people, throughout the world today. Schizophrenia and psychosis has captured the headlines increasingly for the past few years.

Anti-psychotic drugs which are in use today, the safety profile is not so promising considering the fact that it has to be continued for a few years. The significant and serious adverse effect of these drugs is the extrapyramidal side-effects, which includes akathesia, acute muscle dystonia, and tardive dyskinesia.[2] Over the long term, these anti-psychotics may cause dopaminergic pathways in the brain permanently dysfunctional.[3] They may lead to severe movement disorders like tardive dyskinesia, tardive psychosis, and global cognitive decline tardive dementia.[2,3] There has been enough evidence as suggested by the recent MRI scans of schizophrenia patients that anti-psychotics even are responsible for the shrinkage of the basal ganglia region of the brain.[3] Keeping all the above facts in mind, this study was done for exploration of the herbal formulations, which can be used for the treatment of schizophrenia patients.

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Demand for herbal drugs is ever-increasing. Herbal drugs are known to have very minimal adverse effect and its well worth a therapy for chronic CNS diseases like psychosis, which is virtually incurable. India is a country where ayurvada has been practiced from the vedic ages successfully. Such an herbal plant is *Alstonia Scholaris,* which belongs to the family Apocynaceae found widely in all parts of India. The leaves and the stem extract (ethanolic) and its fraction have been studied for anti-anxiety, anti-depressant, anti-tussive, anti-asthmatic, and expectorant activities.[4,5] Another herbal plant, *Bacopa Monnieri,* which belongs to the family Schrophulariaceae found widely in all parts of India, has been studied for various CNS activities. The alcoholic extract of *Bacopa Monnieri* is reported to increase the learning performance of rats, and the activity is attributed to saponin mixtures consisting mainly of bacosides A and B.[6] The plant has also been reported to show anxiolytic, anti-epileptic activities.[7,8] Although both the plant have been studied for various CNS ailments, their potential was still unexplored.

This study was focused on evaluation of the neuroleptic activity of the two plant extracts on various animal models of psychosis.

MATERIALS AND METHODS

Plants

Leaves of *Alstonia Scholaris* and *Bacopa Monnieri* were collected from surrounding areas of Durgapur, West Bengal, identified by the department head of Pharmacognosy in Shri Vishnu College of Pharmacy and were kept safely in the herbarium sheet for further reference.

Animals

Wistar Albino rats of either sexes weighing 150-200 gm were obtained from Ghosh Enterprise, Kolkata. They were housed in the animal house of Shri Vishnu College of Pharmacy with the maintenance 12 hrs day and night cycle. They were fed with normal pellet diet with sufficient water *ad libitum*. The study was approved by the institutional animal ethics committee bearing the approval no. 439/PO/01a/CPCSEA. The rats were acclimatized for 7 days prior to the start of the study.

Plant extracts

300 gms of dried and powdered leaves of the *Alstonia Scholaris* were extracted on soxhlet extractor with ethanol for 5 days, whereas 500 gms of dried and powdered leaves of the plant *Bacopa Monnieri* were used for the same extraction process with same solvent. After 5 days, both the extracts were subjected to Rota evaporator to concentrate the extract. Later, it was dried in vacuum to get the completely dried extracts.

Chemicals

Phencyclidine and amphetamine were obtained from the manufacturing company Sigma Aldrich, USA. Pure drug haloperidol was gifted by Crescent Therapeutics Limited, Solan, Himachal Pradesh.

Acute Toxicity Studies

Acute toxicity study was carried out for both the ethanolic extracts following OECD guidelines for testing of chemicals 2001.[9] The ethanolic extract was suspended in water with 2% w/v gum acacia with the dose of 5 mg kg^{1} body weight was orally administered to overnight-fasted, healthy rats ($n = 3$). The animals were observed individually after dosing at least once during the first 30 min, periodically during the first 4 h, with special attention given during the first 24 h and daily thereafter for a total of 14 days. The acute toxicity study was repeated with doses of 50, 300, and 2000 mg kg^{-1} body weight.

Methods

Amphetamine-induced stereotype in rats[10]

Amphetamine is an indirect sympathomimetic agent. It induces licking, gnawing, grooming, sniffing (stereotype) in rats, which can be successfully prevented by classical neuroleptic agents. This test is predictive of anti-psychotic drug, for D2 receptor antagonism. Six groups (n = 6) of adult Wistar rats were taken weighing between 180 to 220 gm and were treated with either test or the standard drug Haloperidol (0.2 mg/kg) and then placed in individual cages. They were injected with d-amphetamine (5 mg/kg ip) after 30 mins. The onset of stereotypic behavior was evaluated at 30 mins interval for 3 hours. The reduction in mean stereotype score is indicative of anti-psychotic effect.

Phencyclidine (pcp)-induced bizarre pattern of locomotor activity[11]

Phencyclidine is a glutamate receptor antagonist. Administration of phencyclidine has been found to induce locomotor hyperactivity in rodents and is antagonized by anti-psychotic drugs. Male Wistar rats weighing 150-200 gm were housed in a chamber. Animals were divided into six groups ($n = 6$), for test or the standard compound. Thirty mins before the start of the experiment, the animals were administered with the extract or the standard drug. Phencyclidine (2 mg/kg) was administered to the animals of both the groups just before the start of the experiment. Then, the locomotor activity of the animals was measured in photoactometer for a session lasting for 90 mins. Drugs antagonizing the phencyclidine-induced activity are expected to act by some other receptor *viz.* glutamatergic and serotonergic rather than dopaminergic receptors.

Phencyclidine (pcp)-induced social withdrawal test[12]

This test helps to show the effectiveness of potential anti-psychotic drugs against negative symptoms of schizophrenia. Phencyclidine decreases the time of social interaction in the rats. Naïve male Wistar rats were housed in pairs for 10 days prior to the start of the experiment. During the test, one cage mate was removed, and a new one was kept in the cage for 20 mins. The amount of social interaction was measured as the total amount of time spent on various elements of interaction i.e., social exploration and genital investigation. Phencyclidine was administered 5 mins before the start of the experiment, whereas the test or the standard drug was given 30 mins before the experiment.

Conditioned avoidance response in rats[12]

Perhaps the oldest animal model to predict potential anti-psychotic drug efficacy is the conditioned avoidance response (CAR). In the conditioned reinforcement model, experimental animals were trained to perform a certain response i.e., to avoid a mild shock. Trained avoidance responses may be active (pressing a lever, climbing a pole, or jumping out of a box). Classical anti-psychotic drugs reduce avoidance responding at doses that do not impair natural (untrained) escape. Six groups of rats weighing 150-250 gms were tested in this model for test drug or standard. Ten days of training period were carried out before the experiment, and a total of 20 sessions of training were imparted to each rat before the experiment. Test or the standard drugs were administered 30 mins before the start of the experiment.

Induction of catalepsy in rats[10,12]

Wistar rats weighing 180 to 200 gms each were randomly divided in groups. After an appropriate pre-treatment time of the drug, each rat was tested for with respect to the right and left front paws, which are first put on columns, first 3 cm and then 9 cm high. The cataleptic state was considered if the rat maintains the abnormal posture for 10 sec or more. The scoring was done according to the following:

0- The rat moves normally when placed on a table.

1- Rats move only when touched or pushed.

1 + 1 = 2 – Rats placed on a table with front paws set alternately on a 3 cm high block fails to correct the posture in 10 secs, scored as 1 point for each paw, with a total of 2 for both paws.

1 + 1 = 2 – Rats placed on a table with front paws set alternately on a 9 cm high block fails to correct the posture in 10 secs, scored as 1 point for each paw, with a total of 2 for both paws.

This model predicts the extrapyramidal side-effects of the test drug.

Estimation of dopamine in different regions of the brain[13]

The following day of drug administration, the rats were decapitated and the brains were removed immediately according to the method described by Glowinski and Iversen.[14] The striatum and the frontal cortex regions were removed and were immediately frozen on dry ice and stored at -80°C. Striatal and frontal cortical tissues were sonicated in 0.1 M of perchloric acid (about 100 µl/mg tissue). The supernatant fluids were taken for measurements of levels of dopamine by HPLC. Briefly, 20 µl of supernatant fluid was isocratically eluted through a 4.6-mm C18 column containing paracetamol (100 mg/ml) as the internal standard with a mobile phase containing 50 mM ammonium phosphate pH 4.6, 25 mM hexane sulfonic acid pH 4.04, and 5% acetonitrile and detected by a UV spectrophotometer detector. The flow rate was 1 ml/min. Concentration of DA was expressed as nanograms per gram of tissue.

Statistical analysis

All the values were expressed as mean ± SEM. Data analysis will be with the help One-way Anova followed by Students *t* test as when required.

Groupings of the animals

Control Group – Animals of this group received 2% Gum acacia suspension.

Group II – Animals of this group received standard drug (Haloperidol).

Group III – Animals of this group received *Alstonia Scholaris* (ALS) extract at a dose of 100 mg/kg.

Group IV – Animals of this group received *Alstonia Scholaris* (ALS) extract at a dose of 200 mg/kg.

Group V – Animals of this group received *Bacopa Monnieri* (BM) extract at a dose of 100 mg/kg.

Group VI – Animals of this group received *Bacopa Monnieri* (BM) extract at a dose of 200 mg/kg.

The animals were administered with test extracts drug orally with the help of oral feeding tubes and standard drug intraperitoneum route.

RESULTS

Extraction

The amount of the extract obtained for *Alstonia Scholaris* and *Bacopa Monnieri* plants were 22% and 10%, respectively, of the initial material for each plant.

Acute toxicity studies [Table 1]

Both the ethanolic extract of both the plants was found to be safe up to the dose of 2000 mg/kg body weight. Accordingly, 1/10th and 1/20th of the lethal dose were

selected for the study was 100 mg/kg and 200 mg/kg body weight for each of the extracts.

Amphetamine-induced stereotypy in rats [Table 2]

Results from this study shows that all the stereotypic activities like sniffing, rearing, and licking were reduced significantly in all the treatment groups ($P < 0.05$) compared to the control groups, but the degree of reduction varied differently among the treatment groups with no significant difference among the different doses of both the extracts. The standard drug haloperidol reduced sniffing, rearing, and licking activity by 65%, 55%, and 50%, respectively. The ethanolic extract of ALS reduced sniffing, rearing, and licking activity by 35%, 43%, and 27%, respectively, whereas the BM extract reduced sniffing, rearing, and licking activity by 22%, 20%, and 17%, respectively, compared to the control groups.

Phencycline-induced bizarre pattern of locomotor activity [Table 3]

Results from this model were suggestive of no significant change in the locomotor activity for all the treatment groups compared to the control group. This result also suggests that both ALS and BM and the standard drug did not alter the locomotor activity at any of their doses used.

Phencyclidine (PCP)-induced social withdrawal test [Table 4]

No animals from the test groups (ALM and BM) or the standard group altered the social exploration and the anogenital inspection activity compared with the control group significantly ($P > 0.05$). This model is suggestive of the absence of negative symptoms alleviating property of all the treatment groups.

Conditioned avoidance response in rats [Table 5]

All the groups significantly decreased the escape response compared to the control group ($P < 0.05$). Group II reduced the escape response by almost 70%, Group III and IV by 44%, and Group V and VI by 25%. However, there was no dose-dependent reduction of escape response for both the ALS and the BM extract.

Induction of catalepsy in rats [Table 6]

All the treatment groups increased the mean cataleptic scores significantly ($P < 0.05$) compared with the control group. However, the increase in mean cataleptic score was increased by almost 100% in case of the test extract, whereas 300% in case of the standard drug haloperidol. However, most the animals of the ALS- and the BM-treated groups corrected their stretched limb position within 10 seconds, but they needed a touch or some kind of push for their movement to start. There was no significant difference in cataleptic score among the different dose group of the two test extracts.

Estimation of dopamine in different brain regions [Table 7]

The dopamine estimation in the 2 regions of the brain suggested that the dopamine levels decreased in the frontal cortex for all the treatment groups including the standard, but the decrease in dopamine concentration was more for the standard drug than the ALS and the BM extract when they were compared with the control. However, there were no significant changes in the striatum dopamine levels of the animals treated with the ALS or the BM extract when compared with the control, but there was a significant alteration in dopamine levels in the standard group when compared with the control group.

Table 1: Acute toxicity studies

Dose	5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
No. of animals	3	3	3	3
No. of animals dead	Nil	Nil	Nil	Nil

Table 2: Inhibition of amphetamine-induced stereotype

Groups	Sniffing	Rearing	Licking
Control	8.3±1.15	5.52±0.94	3.7±0.28
II	2.9±0.28#	2.44±0.16#	1.62±0.20#
III	5.23±1.16#	3.25±1.60#	2.82±0.23#
IV	5.67±2.20#	3.26±1.69#	2.74±0.36#
V	6.62±1.78#	4.46±0.77#	2.98±0.52#
VI	6.50±1.99#	4.40±0.63#	2.69±0.66#

N=6; #= *P*<0.05 when compared with control

Table 3: Phencyclidine-induced bizarre pattern of locomotor activity

Groups	Locomotor activity scores
Control	302±7.28
II	300±6.23
III	299±12.70
IV	303±5.28
V	302±6.87#
VI	299±8.19#

N=6; #=*P*>0.05 when compared with control

Table 4: Phencyclidine-induced social withdrawal test

Groups	Social exploration	Anogenital inspection
Control	8±0.81	3±0.81
II	7±1.58$	3±1.63$
III	8±0.70$	2±1.92$
IV	8±2.29$	2±1.66$
V	7±0.78$	2±1.87$
VI	7±1.15$	3±088$

N=6; $=*P*>0.05 when compared with control

Table 5: Conditioned avoidance response in rats

Groups	No. of times escaped
Control	16±0.95
II	4.8±1.23#
III	9±1.64#
IV	9±0.97#
V	11±1.98#
VI	12±0.73#

N=6,#=*P*<0.05 when compared with control

Table 6: Induction of catalepsy in rats

Groups	Mean cataleptic scores
Control	0
II	3.46.±0.35#
III	1.02±0.12#
IV	1.24±0.12#
V	1.09±0.27#
VI	0.98±0.23#

N=6; #=*P*<0.05 when compared with control

Table 7: Estimation of dopamine in different regions of the brain

Groups	Frontal cortex (ng/gm)	Corpus striatum (ng/gm)
Control	0.45±0.04	11.99±1.36
II	0.27±0.02#	8.42±2.52#
III	0.37±0.07#	10.11±1.62
IV	0.34±0.03#	10.24±0.58
V	0.32±0.07#	11.96±1.56
VI	0.35±0.03#	11.64±1.02

N=6; #=*P*<0.05 when compared with control

DISCUSSION

Improving the effectiveness of anti-psychotics appears to require proper and specific modulation of the various DA pathways. For instance, lessened extrapyramidal symptoms observed with newer agents are thought to be consequent to differential effects on the striatum and frontal cortex, respectively.[15]

Haloperidol and ethanolic extract of leaves of ALS and BM showed decrease in amphetamine-induced stereotype compared to the control group. However, the extent of decrease of the stereotypic activity for AS and BM was less as compared to the standard drug haloperidol. This kind of outcome was indicative of a possibility that the test extracts may be decreasing the labels of dopamine levels in the brain as is the case for the standard drug haloperidol.[10]

Neither of the test extracts or the standard drug altered the phencyclidine-induced increase in locomotor activity. Ineffectiveness of the extracts to show any effect on this model suggested that the extracts may not be acting on other neurotransmitter systems like glutamatergic or serotonergic.[11]

Both the extracts along with the standard drug did not have any impact on the phencyclidine-induced social interaction test. This particular model was suggestive of the ineffectiveness of the test extracts to alleviate the negative symptoms of schizophrenia.[11] It is once again established that haloperidol has no effect on the negative symptoms of schizophrenia.

Both the extract as well as the standard drug reduced the conditioned avoidance response; however, the magnitude of reduction was less for the test extract than the standard drug when they were compared with the control group. This kind of results for the standard and the test extracts again indicated the alleviating effects of positive symptoms of schizophrenia.[12]

The induction of catalepsy once again pointed out the fact that both the extracts like the standard drug could be acting on the dopaminergic neurons of the brain.[12] Haloperidol is known to decrease the dopamine levels on various dopaminergic pathways of the brain, which is the reason for extra pyramidal motor disorders.[16] Further analysis of the data showed that there were no significant dose-dependent effects for both the extracts in decreasing the dopamine levels.

The reduction of the dopamine level in the frontal cortical regions of the brain was a kind of confirmatory result to establish the mode of anti-psychotic action of the test extracts. This was a major finding of the study, which was indicative and assertive of the mode of action of the *Alstonia Scholaris* and the *Bacopa Monnieri* extracts. However, the dopamine-lowering activity for both the extracts was less, when compared to haloperidol.

Nevertheless, the unchanged dopamine level in the corpus striatum for both the extracts irrespective of the dose was also a significant observation for this study. This observation was pinpointing the fact that the test extracts may not affect any kind of motor incoordination like that of the typical neuroleptic drugs.[17] However, the extracts of ALS and BM have shown the signs of catalepsy (in the animal model), although its magnitude was very less. Further studies are required in this context, although it can be argued that majority of the neuroleptic have considerable amount of sedative action, and this can be mistaken for cataleptic activity as seen in the animal model when most of the animals moved on the table only when touched or pushed.[17,18]

Taking all the above facts into consideration, it may be safe to say that the ethanolic extract of the leaves of *Alstonia Scholaris* and *Bacopa Monnieri* decreases the dopamine levels in the frontal cortical regions of the brain.

The dopamine-lowering effects of the extracts were less than the standard drug, but the encouraging fact was that the extracts did not alter the level of dopamine in the striatum region of the brain. This indicates the possibility of reduced extrapyramidal effects of the extracts, and in this context, it may be superior to the standard drug. Nevertheless, chronic toxicity studies need to be carried out considering the prolonged use of the extracts.

It was already recognized earlier that even the drugs having less affinity for the dopaminergic receptor than haloperidol, do have acceptable anti-psychotic symptoms alleviating effect.[19] Its also well-established that it is extremely essential for a molecule to have dopamine antagonistic activity to have any kind of neuroleptic activity.[20] Even the atypical anti-psychotic drugs discovered later need to have a certain degree of dopamine-reducing activity apart from its interaction with other receptors *viz.* serotonergic, alpha adrenergic, or histaminergic.[21,22] So, it can be stated that by virtue of the dopamine-lowering effect of the ALS and the BM extract in the frontal cortical region of the brain, they possess the anti-psychotic effects. Moreover, the results of the phencyclidine-induced social interaction test pointed out the fact that the extracts may not be altering the serotonin levels of the brain.

CONCLUSION

The two herbal extracts used have shown promising effects in this study in reducing the positive symptoms of psychosis in rats by reducing the dopamine levels in the frontal cortical region of the brain. These extracts can be further isolated to find out the active constituents responsible for this kind of activity, which can also be major area of further research.

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REFERENCES

1. Hafner H, Heiden W. Epidemiology of schizophrenia. Can J Psychiatry 1997;42:139-51.
2. Lieberman JA. Effectiveness of antipsychotic drugs in patients with chronic Schizophrenia. N Engl J Med 2005;353 Suppl 12:S1209-17.
3. Roth BL, Tandra S, Burgess LH. D4 receptor affinity does not distinguish between typical and atypical antipsychotic drugs. Psychopharmacology 1995;120 Suppl 3:S332-7.
4. Arulmozhi S, Mazumder PM, Sathiyanarayanan L, Thakurdesai A. Anti-anxiety and anti-depressant activity of leaves of alstonia scholaris. Pharmacologia 2012;3 Suppl 8:S239-48.
5. Shang JH, Cai XH, Zhao YL, Feng T, Luo XD. Pharmacological evaluation of Alstonia Scholaris. Antitussive, antiasthmatic and expectorant activities. J Ethnopharmacol 2010;129 Suppl 3:S293-8.
6. Roodenrys S. Chronic effects of Brahmi (Bacopa Monnieri) on human memory. Psychopharmacology 2002;27 Suppl 2:S279-81.
7. Wadodkar SG, Achliya GS, Dorle AK. Evaluation of CNS activity of Brahmi Ghrita. Indian J Pharmacol 2005;47 Suppl 1:S33-6.
8. Kaushik D, Tripathi A, Tripathi R, Ganachari M. Anticonvulsant activity of Bacopa Monnieri in rodents. Braz J Pharm Sci 2009;45 Suppl 4:S643-9.
9. OECD. Guidance document on Acute Oral Toxicity. Environmental Health and safety monograph series on safety and assessment No. 24, 2001.
10. Kulkarni SK, Dandiya PC. Influence of intraventricular administration of norepinephrine, dopamine and 5-hydroxytryptamine on motor activity of rats. Indian J Med Res 1975;63:462-8.
11. Corbett R, Camacho F, Woods AT, Kerman LL, Fishkin RJ, Brooks K, *et al.* Antipsychotic agents antagonize non-competitive N-methyl-D-aspartate antagonist-induced behaviors. Psychopharmacology (Berl) 1995;120:67-74.
12. Matthysse S. Animal models in psychiatric research. Prog Brain Res 1986;65:259-70.
13. Cleren C, Calingesan NY, Chen J. Celesterol protects against MPTP and 3 nitro propanoic acid induced neurotoxicity. J Neurochem 2005;94:995-1004.
14. Glowinski J, Iversen L. Regional studies of catecholamine in Rat brain. J Neurochem 1966;13:655-69.
15. Baldessarini R. Drugs used in the treatment of Psychiatric disorder. In: Hardman J, editor. 10th ed. Goodman Gilman's Pharmacological basis of Therapeutics. Tennessee: McGraw Hill; 2001. p. 789-896.
16. William P, Hollister L. Antipsychotic agents and Lithium. In: Katzung BG, editor. 10th ed. Basic and Clinical Pharmacology. San Francisco: McGraw Hill; 2007. p. 457-63.
17. Turner. A. Ataractic Agents. 1st EditionScreening methods in Pharmacology. New York: Demic Press; 19651. p. 87-99.
18. Raymond B, Neumeyer J. Antipsychotics and Anxiolytic agents. In: Troy DA, editor. 5th ed. Foyes Principles of Medicinal Chemistry. Philadelphia: Lippincott; 2002. p. 408-33.
19. Rang HP, Dale MM, Ritter JM, Flower RJ. Antipsychotic agents. 7th ed. Pharmacology Philadelphia: Elsevier; 2007. p. 455-69.
20. Anthony A, Martin R, Thurkauf A. Antipsychotic drugs. In: Abraham DJ, editor. 6th ed. Burgers Medicinal Chemistry and Drug Discovery. Virginia: Willey Interscience; 2003. p. 599-672.
21. Green M. What are the functional consequences of neurocognitive deficits in schizophrenia? Am J Psychiatry 1996;153 Suppl 1:S321-30.
22. Goldberg TE, Gold JM, Braff DL. Neuropsychological functioning and time-linked information processing is schizophrenia. Rev Psychiatry 1991;10:601-13.

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