ANTIPSYCHOTIC EFFECT OF AQUEOUS STEM BARK EXTRACT OF *Amblygonocarpus andongensis* IN WISTAR ALBINO RATS

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ABSTRACT

The study of antipsychotic effect of the aqueous stem bark extract of Amblygonocarpus andongensis was carried out on amphetamine induced psychosis in 42 Wister albino rats weighing between 105 and 305.2g using two indices: feeding and locomotor activity. Twelve out of the 42 rats were divided into two groups; six per group. Group 1 and 2 received 1.5mg/kg body weight of oral amphetamine. Oral chlorpromazine (0.5mg/kg) was administered to group 2 rats in addition. The remaining 30 rats were divided into 5 groups: A, B, C, D, and E, each group comprised 6 rats. All the groups received 1.5 mg/kg body weight of amphetamine but E received 0.5mg/kg oral chlorpromazine in addition. However, B, C and D received 450, 900 and 1350mg/kg bodyweight of Amblygonocarpus andongensis aqueous stem bark extract. Feeding and locomotor activities were measured in groups 1 and 2 and A, B, C, D and E rats respectively. The result showed that there were significant differences in feeding and locomotor parameters between groups 1 and 2 and among groups A, B, C and E ($p<0.05$) except group E. In amphetamine psychotic model test, group 2 animals have reduced feeding and locomotor activity as compared to group 1. Conclusively, Amblygonocarpus andongensis has a dose dependent reducing effect on feeding and locomotor activity at 135mg/kg body weight as compared to chlorpromazine (0.5mg/kg) in amphetamine induced psychosis in Wister albino rats. Hence both Amblygonocarpus andongensis and chlorpromazine may have pharmacokinetic effect on amphetamine and therefore maybe used to treat psychosis induced by amphetamine.

Keywords: Antipsychotic, effect, Amblygonocarpus, andongensis, Wister rat

INTRODUCTION

Psychosis is the term used to describe a mental state in which the individual experiences a distortion or loss of contact with reality, clouding of consciousness (Joel *et al.,* 1996). The mental state is characterized by the presence of features such as depression, anxiety, sleep disturbance, social withdrawal and impaired role functioning during a psychotic episode (Joel *et al.,* 1996). Psychosis can be caused by a number of conditions. These include organic causes such as drug intoxication, metabolic and schizoaffective disorder (Szasz, 1960).

Psychotic mental illnesses are of major social and public health importance. These conditions affect a significant number of individuals in our communities. About two percent of people experience a psychosis episode at some stage in their life (Beekman *et al.,* 1999). An estimated 80 % of those affected by psychotic disorder experience their first episode between the ages of 16 and 40 years (Beekman *et al.,* 1999). It has been postulated that the onset of course of psychosis is determined by an underlying vulnerability of psychosis coupled with the impact of environmental stresses, which may then trigger active psychotic symptoms. This is the so-called stress/vulnerability model for psychosis (Ayd and Blackwell, 1970).

The use of drugs is the most important in the management of psychosis (Ross, 1996). The current effective antipsychotic agents are tricyclic antidepressants such as: phenthiazines, thioxanthenes, benzodiazepines, as well as butyrophenones and its congeners. Other drugs include heterocyclic and experimental benzamides (Ross, 1996). All these drugs block D_2 dopaminergic receptors and inactivate dopamine neurotransmission in the forebrain. Some also interact with D_1

dopaminergic, $5HT_2$ serotonergic and alpha-adrenergic receptors (Ross, 1996). Although low potent chlorpromazine has more sedative, hypertensive and autonomic side effects (Ross, 1996).

Because of side effects of these antipsychotic drugs, there is need to investigate our indigenous herbs that have long standing claims of antipsychotic properties by our indigenous traditional medical practitioners. More so, Orji *et al.,* (2003) reported that Nigeria has an interesting rich flora ranging from mangrove swamps and rainforest in the south to the savanna and thorn bush regions in the north.

Since there has been a renewed interest in the use of traditional medicine in the last decade (Ross, 1996), the need to investigate our indigenous plants for the antipsychotic properties is not out of place. Therefore, this study was designed to investigate the antipsychotic effect of aqueous stem bark extract of *A. andongensis* in wistar albino rats.

MATERIALS AND METHODS

Plant Materials: *A. andongensis* stem bark used for the experiment was collected from Anka town in Zamfara State, and identified by a botanist in the herbarium of Biological Science Department, Usmanu Danfodiyo University, Sokoto, Nigeria where a Voucher specimen was kept. The stem of the plant was washed and the bark separated, air-dried and pulverized using mortar and pestle.

Extraction: One hundred (100) grammes of the pulverized air-dried bark of *A. andongensis* was dissolved in 500 mls of distilled water in a conical flask. The mixture was shaken vigorously for 6 hours and allowed to stand for 24 hours. It was then filtered with Whatman (No. 1) filter paper and the filtrate was evaporated at 50^{o} C in a desiccator (Eduardo *et al.,* 2000).

Experimental Animal: Forty-two (42) Wistar albino rats of either sex weighing between 105 to 305.2 g were used for the study. They were acquired from the Animal house, Zoological Garden, Usmanu Danfodiyo University, Sokoto and housed in cages in Pharmacology Department Research Laboratory. They were acclimatized for two weeks, fed on pellets of growers marsh poultry feed (Vital feeds®) and allowed access to water. Twelve out of the 42 rats were used to test for psychotic model of amphetamine. Whereas the remaining 30 rats were used for psychotic and antipsychotic model of amphetamine and *A. andongensis* respectively.

Confirmation of Amphetamine as Psychotic Model: The method of Oscar *et al.* (2004) was adopted. Twelve out of the 42 rats of either sex were divided into two groups, 1 and 2. After having weighed each of the twelve rats, the rats in group 1 and 2 were treated orally with 1.5 mg/kg body weight of amphetamine and their physical, somatic locomotive and behavioral responses were observed and recorded. Stereotype locomotive activity such as sudden quick, jerky movement (agitation) and feeding habits were recorded (Psychotic model). The rats from group 2 received chlorpromazine at 0.5mg/kg 30 minutes post administration of amphetamine but they were observed for abnormal behaviors (Antipsychotic model). This was to access the reliability of the models used for the experiment.

Antipsychotic Test with *Amblygonocarpus andongensis* Aqueous stem bark Extract: Thirty (30) Wister albino rats of either sex weighing between 105 g and 305.2 g were randomly distributed into 5 groups of 6 animals per group, labeled A (negative control), B, C, D, and E (positive control).

The rats from group A - E were treated orally with amphetamine to induce psychosis at the dose of 1.5 mg/kg body weight using a blunt ended canula. After the induction of psychosis in all the 30 rats, the rats in group B - D were treated with 450, 900 and 1350 mg/kg of the extract and the group E rats received chlorpromazine at the dose rate of 0.5 mg/kg body weight 30 minutes post amphetamine administration. The physical, somatic and behavioral changes observed from all the groups were recorded.

Statistical Analysis: The data were analyzed using one-way ANOVA followed by Turkey Kremer's multiple comparison tests (Petrie and Watson, 2002).

RESULTS

Confirmation of Amphetamine as Psychotic Model: Less than 10 minutes post administration of 1.5 mg/kg body weight of oral amphetamine, all the rats from groups 1 and 2 showed behavioural and somatic changes. There were repetitive stereotype locomotive activities, reduction in general activity level, anorexia, reduced feed intake, pupilary dilation and recumbency. But in group 1, appetite was restored 271.17 $\pm$ 1.2 minutes post administration of amphetamine but group 2 had reduced duration of action of psychotic effects characterized by agitation and loss of appetite that was restored after a short period of time (144.5 $\pm$ 1.34 min) as compared to those of group 1 (271.17 $\pm$ 1.2) (Figure 1.)

Anti-psychotic Effect of *Amblygonocarpus andongenesis* Aqueous Stem Bark Extract: The results of antipsychotic effect of *andongensis* extract in wistar albino rats revealed significant difference ($P < 0.05$) in parameters (feeding and agitation) among groups A, B and C, except group D that received highest dose of the extract and group E that received chlorpromazine where the differences were not increased significantly ($P > 0.05$) (Table 1). Nevertheless, *andongensis* extract started showing antipsychotic effect using feeding as a parameter 204.5 $\pm$ 2.5, 190.1 $\pm$ 0.7 and 150 $\pm$ 1.0 min post administration of the extract in groups A, B and C respectively (Figure 2). But onset of action of the extract and chlorpromazine in group D and E rats were 150 $\pm$ 1.0 and 145 $\pm$ 2.21 minutes respectively.

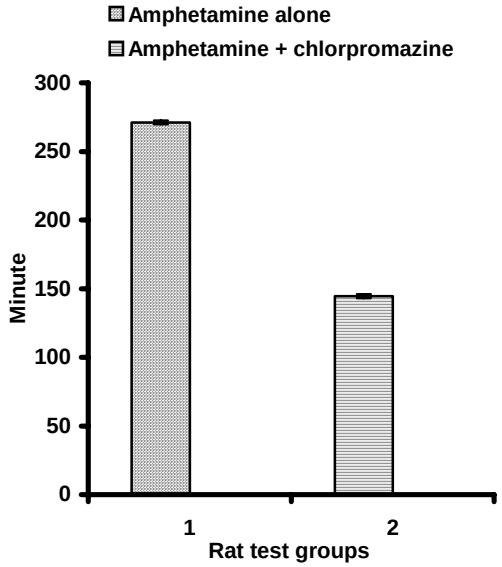

Figure 1: Atenuating effect of chlorpromazine on amphetamine induced psychosis (using feeding and agitation)

The effect of the extract lasted for about 65 ± 3.11, 80 ± 2.34, 120.17 ± 2.56 and 125 ± 2.61 minutes in animals of groups B, C, D and E respectively (see table 1 fig 2). The periods taken before restoration of appetite were 270 ± 3.03, 205 ± 2.38, 90.17 ± 2.71, 149.83 ± 2.01 and 145 ± 2.2 minutes in groups A, B, C, D and E respectively (Table 1).

Table 1: Antipsychotic Effect of *Amblygonocarpus andongensis* in Albino Rats Using Feeding Parameter

Parameters	Experimental rats				
	A	B	C	D	E
Onset of action (min)	-	204.5 ± 2.4	190.1 ± 0.7	150 ± 1.0*	145 ± 2.21*
Duration of action (min)	-	65 ± 3.11	80 ± 2.34	120.17 ± 2.56*	125 ± 2.61*
Restoration of appetite (min)	270 ± 3.03	205 ± 2.38	90.17 ± 2.71	149.83 ± 201*	145 ± 2.2*

Key: P > 0.05; A = Amphetamine; B = Amphetamine + 450 mg/kg of extract; C= Amphetamine + 900 mg/kg of extract; D = Amphetamine + 1350 mg/kg of extract; E = Amphetamine + Chlorpromazine*

DISCUSSION

The observation of the increased stereotyped locomotory activity (in form of quick, sudden movement, sudden halting and restlessness), anorexia upon administration amphetamine to group 1 and 2, and A - E rats (fig. 1 and 2) agreed with what Mark and Athina (2000) reported. They reported that amphetamine can induce psychotic activities in animal models. However, in group 2 animals feeding and agitation were reduced 150 minutes post chlorpromazine administration. But group 1 animals resumed feeding 271 minutes post amphetamine administration.

In the phase of the antipsychotic testing of the extract, the rats in group A (amphetamine alone) went off feed immediately, and could not resumed feeding until after 270 ± 3.03 minutes (Table 1). The result is in concordance with what was obtained (271.17 ± 1.2) in group 1 animals that were used to confirm the reliability of amphetamine model of psychosis in this experiment. This also agrees with the finding in human that weight loss in obesity following amphetamine treatment is almost entirely due to its anorectic effect but also due to increased metabolism (Joel *et al.,* 1990).

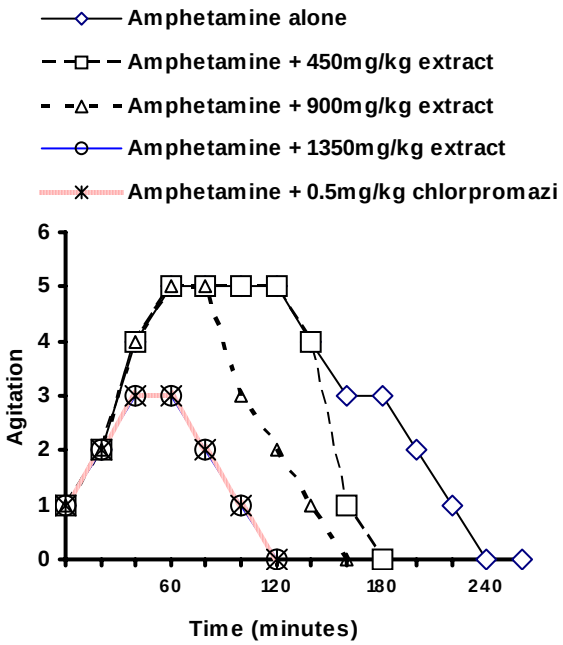

Figure 2: Antipsychotic effect of Amblygonocarpus andongensis using agitation parameter

The resumption of feeding 270 minutes post amphetamine treatment agrees with the observation of Silverton (1992) and Bray (1993) that tolerance to amphetamine is very rapid and thus continuous quest for higher dose. The decrease from 270 to 205 minutes in period of anorexia in group B rats given 450 mg/kg of the extract was significant (P<0.05) suggesting the antianorexic effects of the extract even at low doses. The group C and D rats that received 900 and 1350mg/kg limit doses of the extract recorded significant decrease in duration of restoration of appetite (P < 0.05). The restoration of appetite of the group E rats that received chlorpromazine (0.5 mg/kg orally) following 1.5 mg/kg oral amphetamine treatment was not statistically significant as compared to those of group D (P > 0.05) (Table 1).

Also, agitation of the rats reduced in duration with increase in the dose of the extract following amphetamine administration. Group D animals (1350 mg/kg) firstly becoming calmed and

lastly group B. That is as the dose of the extract increased, the period of calming effect also increased.

The highest antipsychotic effect (agitation) displayed by amphetamine (Fig. 2) for a period of 160 minutes at a dose rate of 1.5mg/kg body weight agrees with the report of Lees (1991) that the effect of amphetamine on the central nervous system (CNS) includes increase alertness (agitation), wakefulness and feeling of euphoria in man. He reported that the application of the agitative effect of amphetamine has been in the treatment of overdose with CNS depressants i.e. analeptic effect. So because of the agitative effect of amphetamine, physical work capacity is improved and sleep is prevented (Lees, 1991). The psychotic effect shown by amphetamine in our study is supported by the report of Tripathy (2003) that alertness, increase concentration, attention span, talkativeness, euphoria and increased work capacity are the central effects of amphetamine as fatigue is allayed.

Nonetheless, the uniformity in antipsychotic effects of chlorpromazine in group 2 and E may be suggestive of the pharmacokinetic effect of chlorpromazine and andongensis on amphetamine as shown by subsequent decrease in psychotic effect of amphetamine in wistar rats (Figures 1 and 2). However, the decrease in the psychotic effect of amphetamine due to Amblygonocarpus extract administration at 450, 900 and 1350 mg/kg in groups B, C and D may suggest the antagonistic effect of the extract of *A. andongensis* aqueous stem bark on amphetamine. Hence, it is used in the treatment of psychosis by the tradomedical practitioner of Northern Nigeria.

Conclusion: In conclusion, the aqueous stem bark extract of *Amblygonocarpus andongensis* has dependant antipsychotic effect at a rate of 1350 mg/kg body weight in comparison with chlorpromazine (0.5 mg/kg). Although, chlorpromazine is more potent than *Amblygonocarpus andongensis.* More so, both chlorpromazine and andongensis may have pharmacokinetic effect on amphetamine.

REFERENCES

AYD. F. J. and BLACKWELL, B. (1970). *Discoveries in biological psychiatric.* J. B. Lippincott Company, Philadelphia.

BEEKMAN, A. T. F., DEEG, D. J. H. and BRAAM A. N. (1999). Consequences of major and minor depression in later life. A study of disability, well-being and service utilization. *Psychological Medicine,* 27: 307 – 311.

BRAY G. A. (1993). Use and abuse of appetite-suppressant drugs in the treatment of obesity. *Annals of Internal Medicine,* 114: 707 – 713.

EDUARDO, G., IRENE, I., EMILIA, C. and ANGEL, V. (2000). Antipsychotic effect of aqueous stem bark extract of *A. andongensis* in wistar albino rat. *Journal of Ethnopharmacology*, 70: 329 – 333.

JOEL, E. H. LEE E. L., PERRY B. M., RAYMOND W. R. and ALFRED, G. G. (1996). Amphetamine Pages 219 -221. *In:* Goodman and Gilman *The Pharmacological Basis of Therapeutics*, 9th edition,

MARK, A. G. and ATHINA, M. (2000). Animal models for psychiatric disorders. Pages 231 – 234. *In: Psychopharmacology,* 4th Edition, Blackwell Science Limited, United Kingdom

OSCAR P. D., ANSELMO, H., ADRIANA, L. S., DIOGO O. S. and DIOGO R. L. (2004). β-Amyloid treatment of sensitizes mice to amphetamine induced locomotion but reduces responses to caffeine. *Neuro Degenerative Disease*, 1: 38 – 43.

LEES, P. (1991). Central nervous system transmitters and mechanism of action of centrally active drugs. Pages 315 – 327. *In:* BRANDER, G. C., PUH, D. M., BYWATER, R. J. and JENKINS, W. L (Eds.) *Veterinary Applied Pharmacology and Therapeutics.* 5th Edition, Bailliere Tindal, London.

ORJI, E. C., OGBUEZUE, D. C. and ORJI, M. U. (2003). Evaluation of antimicrobial activities of leaf extracts of *Morinda lucida* and *Erythrina senegalensis* for medical uses. *International Journal of Gender and Health Studies,* 1(1): 79 – 83.

PETRIE, A. and WATSON, P. (2002). Hypothesis tests 2-the F-test comparing two variances or more than two means. Pages 90 – 99. *In:* PETRIE, A. and WATSON, P. (Eds.). *Statistics for Veterinary and Animal Science*, Blackwell Science Limited, United Kingdom.

ROSS, J. B. (1996). Drugs and the treatment of psychiatric disorder. Pages 399 – 430. *In:* Gilman and Goodman's The Pharmacological Basis of Therapeutics.

SILVERTON, T. (1992). Appetite suppressants. A review. *Drugs,* 43: 820 – 836.

SZASS, T. S. (1960). The myth of mental illness. T*he American Psychologist,* 15: 113 - 118.

TRIPATHI, K. D. (2003). Drugs used in mental illness: Antipsychotic and anti-anxiety drugs. Pages 390 – 404. *In: Essentials of Medical Pharmacology*, 5th edition. JP Brothers Medical Publishers (P) Limited, New Delhi India.